with the Regards of the Authors
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EXPERIMENTAL RESEARCHES

RELATIVE TO

CORROVAL AND VAO:

TWO NEW VARIETIES OF WOORARA, THE SOUTH AMERICAN ARROW POISON.

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WITH THREE WOOD-CUTS.

THE history of the remarkable poison which we design to consider in the present memoir, has been so well detailed by M. Cl. Bernard,[1] that it would be useless for us to enter fully into this portion of the subject. We shall, accordingly, confine ourselves more particularly to an examination of those accounts which relate to the discovery and mode of preparation of the substance in question, and to the indication of a few statements which have escaped M. Bernard's attention.

Woorara was first introduced to the civilized world in 1595, by Sir Walter Raleigh,[2] on his return from Guiana. The following quotation describes graphically, but with much exaggeration, the action of the poison.

"There was nothing whereof I was more curious, than to finde out the true remedies of these poisonous arrowes; for besides the mortalitie of the wound they make, the partie shot indureth the most insufferable torment in the world, and abideth a most uglie and lamentable death, sometimes dying starke mad, sometimes their bowels breaking out of their bellies, and are presently discoloured as blacke as pitch, and so unsavoury as no man can endure to cure or attend them. and it is more strange to know that in all this time there was never Spaniard, either by gift or torment, that could attaine to the true

[1] Leçons sur les Effets des Substances Toxiques, &c., 1857, p. 238.

[2] Raleigh's Discoverie of Guiana. Printed for the Hakluyt Society. London, 1848.

knowledge of the cure, although they have martyred and put to invented torture I know not how many of them. But every one of these Indians know it not, no, not one among thousands, but their soothsaiers and priests who do conceale it and only teache it but from the father to the sonne."

Garcilasso de la Vega[1] states that the Indians of Peru poisoned their arrows with a species of herb, and that symptoms of poisoning were not produced till about three days after the wound was given; death followed in seven days afterwards, the sufferer raving, eating or gnawing his own flesh, and beating his brains against the wall.

Another kind of poison is spoken of by De la Vega, in which the decomposing matters of human flesh form an important constituent. Previous to the arrival of the Spaniards, the flesh of the natives was employed for this purpose, but conceiving the idea that the flesh of a red-headed Spaniard possessed more heat and virulency than that of their own people, they subsequently employed this material whenever it fell in their way.

De la Condamine[2] states that the poison used by the Indians of South America is extracted by means of heat from the juice of several plants, and especially from certain *lianes* [in Spanish, bejucos, in English, bindweeds]. He asserts that there are over thirty kinds of plants in the Ticunas poison.

Bancroft[3] is more explicit, and gives the following formula for the woorara :—

Bark of the root of the wooraro, six parts;
Bark of the warracobba corra, two parts;
Barks of the root of coranapi baketi, and of hatchybaly, of each one part.

"All these are to be finely scraped and put into an Indian pot and covered with water. The pot is then to be placed over a slow fire that the water may simmer for a quarter of an hour. After which the fluid is to be expressed from the bark by the hands, taking care that the skin is unbroken; this being done, the bark is to be thrown away and the juice evaporated over a moderate fire to the consistence of tar, when it is to be removed.

"The smallest quantity of this poison conveyed by a wound into the red bloodvessels of an animal, causes it to expire in less than a minute, without much apparent pain or uneasiness, though slight convulsions are sometimes seen near the instant of expiration."

According to Fermin,[4] the Indians of Surinam poison their arrows by dipping them to the height of two inches in the juice of a tree called *mancelinier*.

"As soon as an incision is made in this tree, a milky and acrid substance flows out, filled with particles so volatile that the poison is as prompt as violent. It remains active for a long time after the arrows are dipped into it, as I have myself proved in several instances, by shooting animals with arrows which had been poisoned four or five years previously. Death ensued in half an hour after the wounds were inflicted. I have these arrows still in my possession, and

[1] History of Peru. Chapter 37, p. 741.

[2] Relation abrégé d'un Voyage fait dans l'Intérieur de l'Amérique Méridionale, etc. Mémoires de l'Académie des Sciences, t. xii., 1745, p. 391.

[3] Essay on the Natural History of Guiana. London, 1769, p. 288.

[4] Description Générale Historique, Géographique et Physique de la Colonie de Surinam. Amsterdam, 1769, p. 52.

have no doubt that the poison is as active as ever. To show how pernicious it is when recent, the following experiment is adduced :—

"In order to convince the Spaniards, an Indian king wounded a child twelve years of age, slightly in one of the toes, with a poisoned arrow, and immediately ordered the surgeons whom he had summoned, to amputate the limb. This was scarcely done when the Spaniards saw the child expire, not in consequence of the operation, as was fully verified, but from the effects of the poison which was suddenly thrown into the mass of the blood, and had rapidly reached the most important organs, before relief could be afforded."

Humboldt[1] gives a full account of the woorara, and denies many of the absurd statements of previous writers. He was present during the manufacture of the poison at Esmeralda, and states that it is derived from the bark and alburnum of the bejuco de mavacure, a species of bind-weed, belonging to the strychnos family. The fresh juice of this plant is not regarded as poisonous, probably, as Humboldt states, on account of its not being in a concentrated condition. The manner of preparing the poison is as follows :—

"A cold infusion is first prepared by pouring water on the fibrous matter which is the ground bark of the *mavacoure*. A yellowish water filters during several hours, drop by drop, through the leafy funnel. This filtered water is the venomous liquor, but it acquires strength only when it is concentrated by evaporation, like molasses, in a large earthen pot. The Indian from time to time invited us to taste the liquid ; its taste, more or less bitter, decides when the concentration by fire has been carried sufficiently far. There is no danger in this operation, the *curare* being deleterious only when it comes into immediate contact with the blood. The vapours, therefore, which are disengaged from the pans are not hurtful, notwithstanding what has been asserted on this point by the missionaries of the Orinoco."

In order to give body to the extract, another vegetable juice of a very glutinous character is added. The mass thus formed constitutes the curare of commerce.

Another species of the poison prepared entirely from the root is less active.

According to Waterton,[2] the woorara is prepared by the Macousi Indians in the following manner.

The materials required are the woorali vine, a bitter root, one or two bulbous plants, two species of poisonous ants, some strong Indian pepper, and the fangs of the labarri and corra-couchi snakes. Having procured these materials, the Macousi proceeds as follows :—

"He scrapes the woorali vine and bitter root into thin shavings, and puts them into a kind of colander made of leaves ; this he holds over an earthen pot and pours water on the shavings ; the liquor which comes through has the appearance of coffee. When a sufficient quantity has been procured, the shavings are thrown aside. He then bruises the bulbous stalks and squeezes a proportionate quantity of their juice through his hands into the pot. Lastly, the snakes' fangs, ants, and pepper are bruised and thrown into it. It is placed then on a slow fire, and as it boils more of the juice of the woorali is added ac-

[1] Personal Narrative of Travels to the Equatorial Regions of the New Continent during the years 1799–1804. 2d edition. London, 1827, vol. v. p. 519.

[2] Wanderings in South America, p. 51.

cording as it may be found necessary, and the scum is taken off with a leaf; it remains on the fire till it is reduced to a thick syrup of a dark brown colour. As soon as it has arrived at this state, a few arrows are poisoned with it to try its strength."

Schomburgk[1] asserts with much confidence that the woorara is prepared entirely from vegetable substances, the chief of which is the bark of the *strychnos toxifera.* According to this author, the following experiment was instituted by his brother: A gallon of water was added to two pounds of the bark of the *strychnos toxifera,* and allowed to remain for twenty-four hours. Half of the fluid, which was already of a brown colour, was then put into another vessel and evaporated over a slow fire to a syrupy consistence, the remaining half of the fluid being added as evaporation progressed. Two chickens were then wounded with instruments charged with the extract, one in the foot, the other in the neck. Symptoms of poisoning were evident in five minutes. The first died in twenty-seven minutes, the other in twenty-eight minutes after the infliction of the wounds. It is thus shown that the extract of the bark of the *strychnos toxifera* alone, when introduced into the circulation, is speedily fatal.

Schomburgk moreover had an opportunity, as he states, of witnessing the preparation of the woorara by an Indian. According to the account which he gives, three species of the *strychnos* enter into its composition, besides six other plants. No animal matter of any kind was used in its manufacture.

According to Osculati,[2] the poison prepared by the Indians of the province of Esmeralda, and which is called *ciguela* is extracted from a tree, and is not to be compared in virulence with the ticunas. The ciguela will kill a small animal in about ten minutes, but is not fatal when introduced into the human system, causing only pustules and malignant ulcerations. He also refers to another arrow poison prepared by the Colorados.

Osculati[3] also states that the Orekones and Ticunas are celebrated for the manufacture of certain active poisons which kill in two or three minutes. These poisons vary very much in composition among the several tribes. The *ticunas,* or *huarare,* mixed with the *lamas,* a poison prepared by the Lamas Indians, forms a toxic compound fatal to all animals. The ticunas alone is not fatal to quadrupeds or birds. The lamas is considered to be more active, but even this is not fatal to quadrupeds. In a note it is stated that having sent a few small fragments of the poison to Prof. Luigi Patellini, experiments were instituted with it by this gentleman. A guinea pig, poisoned with it, died in about five minutes in tetanic convulsions. The temperature of the body fell at once.

Dalton[4] repeats Waterton's account of the method of manufacturing the

[1] Reisen in Britisch Guiana. Leipzig, 1847. Band i., s. 445 et seq.
[2] Esplorazione delle Regione Equatoriale. Milano, 1850. p. 108.
[3] Op cit., p. 207.
[4] History of British Guiana. London, 1855. Vol. i. p. 68.

woorara, and adds little if any additional information on the subject. He also states, after Hartsinck, that the Indians test the virulence of the poison by shooting arrows charged with it into trees. If the leaves drop off or wither within three days it is deemed sufficiently powerful.

It is highly probable, as Tschudi[1] asserts, that the poison used for weapons by the South American Indians varies with every tribe. This traveller declares that, notwithstanding all assertions to the contrary, animal poisons do enter into the composition of the arrow-poison used by the Indians of Peru. His evidence, however, is only of a hearsay character, as he never witnessed the preparation.

Herndon[2] who, however, does not seem to have paid particular attention to this point, but whose evidence, as far as it goes, is in every way reliable, asserts that the arrow-poison used by the Indians of the Amazon is of a vegetable character, and prepared from the juice of a creeper called *bejuco de ambihuasca* mixed with *aji* or strong red pepper, *barbasco*, *sarnango*, and any other poisonous substances known to the Indians.

Taking the accounts of the several authors we have quoted, as well as the evidence of others who have written on the subject, into consideration, we cannot avoid coming to the conclusion that a great deal of uncertainty still exists relative to the substances and method used in the preparation of the woorara. The earlier accounts on this point are so distorted with manifestly erroneous ideas, and so exaggerated in their detail, that we can place but little reliance upon them. Among later writers, Schomburgk is perhaps more to be depended upon than any other, both on account of general accuracy and high scientific attainments, but it is almost certain that every tribe has its own distinct poison, differing more or less from that of every other tribe. The evidences we have to submit on this point, from our own researches, will, we think, abundantly establish the fact of the different physiological effects resulting from poisoning in the different specimens of woorara, and consequently clearly indicate a difference in composition.

Physical and Chemical Properties.—The woorara obtained by Bancroft[3] is stated by him to have possessed the following properties: It was liquefiable by heat, and dissolvable in water, alcohol, hydrochloric acid and liquor ammoniæ, as also in blood, saliva, &c., except a very small part which subsided both in a spirituous and aqueous menstruum, and consisting, as he thinks, of earthy particles foreign to the composition. It united with acids without emotion or change of colour. On mixing it with alkalies, no ebullition was perceptible, but the colour changed from a reddish brown to a yellowish brown. A few grains mixed with as many

[1] Travels in Peru. English edition. London, 1847, p. 407.

[2] Exploration of the Valley of the Amazon. By Lieut. W. Lewis Herndon, U. S. Navy. Washington, 1853, p. 140.

[3] Op. cit., p. 291.

ounces of human blood, entirely prevented a separation of serum and crassamentum, and the whole mass continued in a state of fluidity.

The first reliable and thorough examination made of the woorara, and one which even yet has not been excelled in completeness, was that of MM. Roulin and Boussingault.[1] The specimen examined by these chemists was obtained from the Rio Negro. It was a solid extract, black, of a resinous appearance, of a brown colour when reduced to powder, and of an intensely bitter taste. This bitterness was unaccompanied by acridity or sharpness. It burned with difficulty, and in consuming gave off no odour of organic nitrogenous substances.

It was but slightly soluble in sulphuric ether, more so in alcohol, forming a beautiful red and very bitter tincture. In water it was soluble to a considerable extent, forming an intensely bitter infusion, of slight acid reaction to litmus paper.

By further investigation, MM. Roulin and Boussingault arrived at the conclusion that no strychnia was present. They, however, obtained an alkaline principle soluble in water, for which the name of *curarin* has been proposed. This substance they obtained by the following procedure:—

The woorara was reduced to powder, and treated repeatedly with boiling alcohol. The alcoholic extract was evaporated, and the residue treated with water, which dissolved the active principle, leaving nothing but a little resinous matter. The aqueous solution was then decolorized by animal charcoal, and treated with infusion of galls. A beautiful whitish-yellow flaky precipitate was thrown down.

The precipitate thus obtained was well washed, heated to ebullition in water, and dissolved by the addition of oxalic acid. The acid liquor was then supersaturated by magnesia and filtered. It was again evaporated to dryness, and the residue dissolved in alcohol. This solution was concentrated and spontaneously evaporated to a syrupy consistence. It was then further concentrated by evaporation *in vacuo*.

Thus obtained, the *curarin* was a solid transparent mass, of an excessively bitter taste, and possessed in an eminent degree of all the virulence of the woorara. It was not crystallizable, was of a pale-yellow colour, and strongly attractive of moisture from the atmosphere. It formed salts with sulphuric, nitric, hydrochloric, and acetic acids, none of which were crystallizable.

MM. Roulin and Boussingault are of the opinion that the normal acid of the woorara is the acetic.

The results of the examination made by the above named chemists were subsequently confirmed by MM. Pelletier and Petroz.[2]

Heintz[3] has also examined the woorara chemically. By adding tannic acid to the aqueous solution of this substance, he obtained an abundant

[1] Examen Chimique du Curare, Poison des Indiens de l'Orinoque. Annales de Chimie et de Physique. Tome xxxix. 1828, p. 24.

[2] Examen Chimique de Curare, Annales de Chimie et de Physique, tom. xl., 1829, p. 213.

[3] Reisen in Britisch Guiana. Von Richard Schomburgk. Band i. s. 452 (note).

precipitate soluble in boiling water. This was taken from the filter, boiled with magnesia, and then evaporated to dryness. The extract thus obtained was then treated with alcohol, to remove it from any insoluble salts of magnesia, and the solution again evaporated to dryness. By this means a yellowish-brown extract was obtained, possessing no alkaline reaction, but endowed in an eminent degree with the toxic principle of the woorara. Heintz does not regard this extract as at all pure. He afterwards employed both the bichlorides of mercury and platinum to effect the precipitation, but with no better success, a yellowish-brown extract being still obtained.

By Lassaigne's method Heintz convinced himself that the extract contained nitrogen. He also found sugar, gum, resin, extractive matter, tannic and gallic acids, and traces of saline combinations with organic acids—probably the tartaric and oxalic.

He was unable to find the least trace of strychnia.

Dr. Brainard,[1] of Chicago, asserts that by an analysis, undertaken at his suggestion, formic acid and a proteinaceous substance were detected in the woorara. None of the details of the analysis are given, and we must therefore await further particulars before accepting such a statement.

Dr. Brainard,[2] in conjunction with Dr. Green, of New York, presented a communication to the French Academy of Sciences, in which the opinion is expressed that the poisonous action of the woorara is probably due to the venom of certain reptiles. Boussingault,[3] however, in the debate which followed, denied the existence of any animal matter in the woorara; and in a subsequent paper, in which the whole subject of woorara is well discussed, Dr. Green[4] doubts the existence of animal poison in the substance in question.

From our own investigations, as well as from those we have referred to, we think it highly improbable that the activity of the woorara is due to animal matters. Doubtless it is true that some Indians introduce the fangs, livers, &c., of venomous reptiles into their arrow poison, but it is scarcely possible that such substances, even if poisonous in the first instance, would retain their activity through the process of manufacture which the woorara undergoes. When we come to detail our own observations, we shall return to this point, so far as it relates to the varieties of this poison with which we have experimented.

Physiology.—The earliest recorded experiments with woorara, of a systematic character, to which we have been able to refer, are those of De la

[1] Smithsonian Report, 1854, p. 123 et seq.

[2] Comptes Rendus, tom. xxxviii., 1854, p. 411 et seq.

[3] Op. cit., p. 414.

[4] American Medical Gazette, vol. vii. No. 1 (new series), Jan., 1858, p. 2, et seq. See also vol. vi. No. 5, May, 1855, and vol. vi. No. 7, July, 1855, for Dr. Green's other important papers on this subject.

Condamine,[1] who relates that his observations were made with arrows which he had possessed for more than a year.

In presence of several high personages a chicken was slightly wounded with a small arrow charged with the poison. It died in seven minutes and a half. Another, pricked in the wing with a similar arrow, died very soon in convulsions, notwithstanding sugar, an alleged antidote, was employed. A third, similarly wounded, recovered, the antidote having been immediately administered. De la Condamine states that age and a low temperature lessen the activity of the poison.

Brocklesby[2] experimented on a cat with the woorara by inoculating the animal with it. The cat expired in about half an hour. An hour afterwards the heart was pulsating, and it continued to beat for two hours after the animal's head was cut off. He found the poison to kill a small bird the moment two drops of it, in solution, were placed on the tongue. He also performed other experiments with it, which, however, do not possess any particular interest.

Herissant[3] instituted a great many experiments on animals with the woorara. Among others is one of, at first sight, considerable importance. He placed a tight ligature around the right posterior leg of a rabbit, and inoculated the animal with the poison of lamas and ticunas below the constriction. The rabbit died in less than ten minutes. In this case it is more than probable that a portion of the poison entered the circulation.

A bear wounded with an arrow dipped into a solution of the poison died in less than five minutes.

He also states that a small boy, to whom he had assigned the task of superintending the evaporation of an aqueous solution of the poison, became sick and faint, but recovered by exposure to fresh air and the administration of a pint of wine and a quantity of sugar. He was himself similarly affected, but recovered by like treatment.

From his experiments he concludes, among many other deductions, that the animals killed with the poison of lamas and ticunas are paralyzed in almost all the muscles before death, and that the muscles are pale and totally deprived of blood.

Fontana's[4] investigations were of a much more philosophical character than those we have referred to, and have formed the basis for most of the succeeding experiments on the subject. He showed conclusively that the vapor of the poison is not deleterious when respired, and thus dissipated one of the ridiculous ideas which had been circulated relative to its action.

[1] Relation abrégé d'un Voyage fait dans l'Intérieur de l'Amérique, Méridionale, etc. Mémoires de l'Académie des Sciences, tom. lxii., 1745, p. 391 et seq.

[2] Letter to the President of the Royal Society. Philosophical Transactions, vol. xliv. part ii., 1747, p. 408.

[3] Experiments made on a great Number of living Animals with the Poison of Lamas and Ticunas. Philosophical Transactions, vol. xlvii., 1751–52, p. 75.

[4] Mémoire sur le Poison Américaine, appellée Ticunas, etc. Sur les Poisons et sur le Corps Animal. Florence, 1781. Tom. ii. p. 83 et seq.

Fontana's experiments are so admirably conceived and carried out, that we think it advisable to lay the main facts of some of them before the Department.

With reference to the action of the ticunas when taken internally, Fontana was the first, we believe, to point out the fact that the state of the stomach at the time of the administration of the poison exercises a most important influence over the result. Thus he found that when the animal's stomach contained a considerable amount of food, death did not follow; but that when this viscus was empty, the animal succumbed, though at a later period than if the substance had been inserted into a wound. Moreover, a larger quantity was required.

He also determined the inefficacy of acids and alkalies as antidotes to the action of the ticunas.

With reference to its effect upon the blood, Fontana found that coagulation was absolutely prevented when a solution of the poison was mixed with it, but that the red corpuscles were not at all modified either in form or size.

He next investigated the action of the ticunas when applied to a nerve entirely isolated from the surrounding tissues. After many careful experiments, he arrived at the conclusion that under such a condition no poisoning is produced.

From additional observations he finally concludes that the ticunas destroys the irritability of the voluntary muscles, but does not affect that of the heart.

We next come to Brodie's[1] researches, which were instituted with woorara brought from Guiana by Bancroft. It was found that after apparent death the heart continued to pulsate for some time, and that its action might be still further prolonged by means of artificial respiration. It was also further ascertained that after division of the nerves supplying the inoculated limb, or ligature of the thoracic duct, the effects of the poison were still produced if the circulation of the blood was not impeded; and hence it was concluded that it is only through this latter channel that the substance in question is capable of exercising its influence. Finally, it was determined that woorara affects the brain by passing into the circulation and acting directly upon the cerebral substance.

In a continuation of the paper quoted, Brodie[2] details the results of further experiments relative to the effects of artificial respiration on animals apparently dead from poisoning with woorara. In one case the animal was perfectly restored to life through the means referred to, notwithstanding the function of the brain had been entirely suspended for a long time.

[1] Experiments and Observations on the different Modes in which Death is produced by certain Vegetable Poisons. Philosophical Transactions, part i., 1811, p. 178 et seq.

[2] Further Experiments and Observations on the Action of Poisons on the Animal System. Philosophical Transactions, part i., 1812, p. 205 et seq.

Waterton[1] also has shown that by means of artificial respiration life may be preserved in animals poisoned with woorara.

Passing over a number of other observations on this subject to which we might refer, we come next to experiments of a later date, performed under more enlightened physiological views, and consequently with more definiteness of purpose. We shall present the main results of these in due order.

Virchow and Münter[2] are the first to whom we have to refer under this head. Numerous experiments were performed by these observers, from which they deduce the following conclusions:—

1. That the woorara, even after having been kept dry for five years, is still intensely poisonous.
2. That the physiological action of the woorara is in harmony with the chemical analysis which denies the presence of strychnia.
3. That woorara therefore does not belong to the class of tetanic poisons, but, like opium, induces stupor; and although it causes slight convulsive actions in cats, there is, nevertheless, neither tetanus nor trismus.
4. That it induces paralysis of the voluntary muscles, with, at the same time, long-continued action of the involuntary muscles (heart, intestines).
5. That woorara does not appear to produce death by absorption from the external surface of the body, but only when it is absorbed through a solution in the continuity of the animal tissues.
6. That in poisoning by woorara, coagulation of the fibrin of the blood ensues in the same manner as though the animal is killed by mechanical means; and that death takes place not so much from any direct result of the poison, but indirectly by its causing the cessation of the respiratory process.

Next in order of publication are the experiments of Bernard and Pelouze.[3] After detailing to some extent the history and physical and chemical properties of the woorara, it is stated that animals poisoned with this substance die without tetanic spasm, there being only a few slight contractions of the muscles of the skin, face, and body.

On examining the bodies of animals poisoned in this manner, it was found that there was a total annihilation of all the properties of the nervous system; the reflex movements were found to be altogether lost; and in animals dead but for a minute, and still warm, the nerves were as inert as though life had been extinguished for a long time. The blood was found constantly black, coagulated with difficulty, and had entirely lost the property of becoming red on exposure to atmospheric air. It is asserted, from these facts, that the action of the woorara is very similar to that of the viper; and that the analogy is still stronger from the circumstance that, like the latter, it may be introduced into the stomach with impunity.

Experiments were then instituted with reference to this last point. In

[1] Experiments with the Woorali Poison; Lancet. Also, American Journal of Pharmacy, N. S., vol. v., 1840, p. 234.
[2] Reisen in Britisch Guiana. Von Richard Schomburgk. Band i. s. 456 (note).
[3] Comptes Rendus, tom. xxxi., 1850, p. 534 et seq.

the first place, it was found that when woorara was mixed with gastric juice, and the solution introduced into the circulation of animals, death uniformly followed. It is, hence, concluded that it is not from any alteration produced by the gastric juice that the poison is innocuous when introduced into the stomach. The other digestive fluids—the saliva, bile, and pancreatic juice—were likewise without effect upon the poisonous properties of the woorara. The inertness of the poison when ingested into the stomach was found to depend upon the fact that the gastric mucous membrane does not allow the toxic principle of the woorara to pass through it.

The following experiment is adduced as tending to establish this view:—

The fresh gastric mucous membrane of an animal (dog or rabbit), recently killed, was adapted to an endosmometer in such a manner that the mucous surface was on the outside. Into the instrument was then placed a solution of sugar in water, and the whole was plunged into an aqueous solution of woorara. At the end of three hours, although endosmosis had been effected, as shown by the elevation of the level of fluid in the tube, it was proven that the liquid contained therein possessed no poisonous quality; showing that the active principle of the woorara had not been transmitted. It was, however, determined that by allowing the arrangement to stand for a long time, the mucous surface became so altered as to permit the endosmosis of the poisonous agent.

It was also shown that the mucous membranes of the bladder, the nostrils, and the eyes were likewise impenetrable to the active principle of the woorara, and that only one mucous membrane of the body, that of the air-passages, was capable of absorbing this substance.

Vulpian,[1] in common with MM. Bernard and Pelouze, also found that the nerves very soon lost their irritability, and that the muscles remained excitable for a considerable period in animals poisoned with woorara. Contrary, however, to the results obtained by these last-named observers, he ascertained that the woorara, when introduced into the œsophagus or stomach of certain animals, as frogs, tritons, and toads, produced death. He also found that when thus administered the heart continued to beat for two or three days, whilst all the nervous functions were entirely abolished. Hence he concludes that the heart is independent of nervous influence.

The experiments of Brainard and Green, to which we have already alluded, will be further considered under another head, as will also the numerous and ably conducted investigations of Reynoso.

In a paper read before the Physiological Society of London, Cogswell,[2] among other conclusions, arrives at the following: That woorara is a poison when swallowed, that it acts primarily as a stimulant, and secondarily, or as it may be termed, specifically, as a sedative, paralyzing the functions of the nervous system both locally, when it is immediately applied to the body, and constitutionally after it enters the circulation.

We now come to Kölliker's[3] investigations, which for thoroughness and

[1] Comptes Rendus de la Societe de Biologie de Paris, t. i., 2d serié, 1854, p. 73.
[2] Lancet, March 3d, 1855.
[3] Physiologische Untersuchungen über die Wirkung einiger Gifte. Virchow's Archiv, Zehnter Band, 1856, s. 83 et seq. For conclusions see also Comptes Rendus, t. xliii. 1856, p. 791, and Proceedings Royal Society of London, 1857.

completeness have rarely been equalled. His conclusions are numerous, and appear to be deduced with his accustomed accuracy.

He found that the woorara acting through the blood destroyed the excitability of the motor nerves, the terminal branches losing their excitability in a few minutes, whilst their trunks did not become affected for an hour or two later. He is of the opinion that the sensory nerves are little if at all affected.

When introduced into the system through the mucous membrane of the intestinal canal, Kölliker found the woorara to act more slowly than through a wound, and that a larger dose was required. When applied to the skin of frogs, he found it altogether inoperative.

With reference to its effect upon the heart, it was determined that in amphibia this organ was but little influenced, as it continued to pulsate for many hours after poisoning was established. Owing to paralysis of the pneumogastric nerves, it was somewhat quickened in its action. He concludes, therefore, that the ganglia remain unaffected. The lymph hearts soon ceased to move.

When applied locally to nerves, woorara in concentrated solution was found to extinguish their excitability, but only after a considerable time. Applied directly to the brain and spinal cord, it was altogether without effect.

The conclusions in regard to the effect of woorara upon the sensory and motor nerves, though published before those of Bernard[1] on the same point, are similar to those which the latter had previously announced in his lectures.

In a second paper Vulpian details the results of further experiments with woorara. He confirms Kölliker's and Bernard's conclusions relative to its action on the nervous system.

He also investigated its effects upon the lymphatic hearts of frogs, and ascertained that under its influence they very soon ceased to beat.

Bernard's most complete researches relative to the action of the woorara are contained in the work to which we have already alluded. As this is so readily accessible to the members of the Department, we shall do no more than present the main results of his investigations. He found,

1st. That all reflex movements cease a few minutes after poisoning. The heart continuing to beat for a considerable time.

2d. That woorara is not absorbed from the mucous membrane of the stomach during digestion, bladder, or from the conjunctiva of mammals, but is readily taken up from the pulmonary and rectal mucous membranes of these animals. When introduced into the œsophagus or gizzard of birds, it is speedily fatal. Applied to the dry skin of frogs, it acts slowly but surely. In contact with the wet skin of these animals, it is not absorbed.

3d. Woorara abolishes the function of the motor nerves, but does not affect that of the sensory nerves. Muscular irritability is rather augmented than diminished.

4th. That woorara kills the nerves from the periphery to the centre, acting in this respect conversely to strychnia.

[1] Leçons sur les Effets des Substances Toxiques et Médicamenteuses.

5th. That it causes death by arresting the process of respiration, thus inducing asphyxia.

The experiments of Prof. E. Pelikan,[1] of St. Petersburg, tend to conclusions similar to those we have last quoted. This observer, however, found that the nervous irritability did not always disappear immediately after death, as stated by Bernard. Prof. Pelikan also found that when introduced into the intestinal canal, woorara exercised its ordinary effect, though more slowly than when acting directly through the circulation. Curarin obtained by the process of Roulin and Boussingault produced the same physiological effect as the woorara.

Having thus brought the history, the chemistry, and the physiology of woorara to the present time, we come, in the next place, to speak of our own researches. These have been conducted with all the care which such observations require. Though we have worked to a certain extent independently, every experiment instituted by one has been verified by the other, so that we are mutually responsible for the statements contained in this memoir. Moreover, observations and suggestions have been freely exchanged.

Original Researches.—The varieties of woorara which we propose to consider were brought, in February, 1857, from the Rio Darien, in the province of New Grenada, South America, by Drs. Ruschenberger and Caldwell, of the United States Navy. By them they were presented to Prof. Joseph Carson, of the University of Pennsylvania, who very generously placed all in his possession at our disposal.

The woorara thus obtained is of two kinds, one marked "*Woorara, variety Corroval,*" is asserted to be the strongest arrow-poison; the other, labelled "*Woorara, variety Vao,*" is not considered so powerful. So far as we are aware, these species of South American arrow-poisons have never yet been noticed by those who have written and experimented upon the subject.

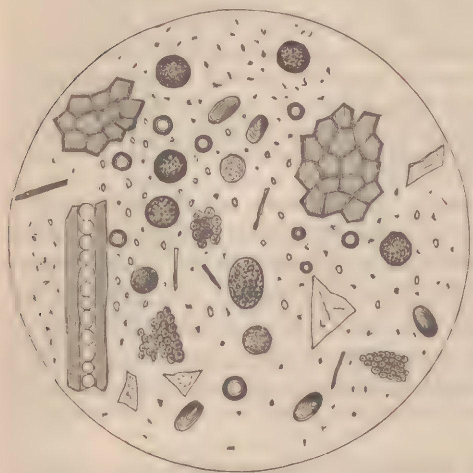
Our friend, Mr. Trautwine, late chief engineer of the Panama Railway, informs us that the arrow-poison employed by the Indians of the Rio Atrato, on the eastern side of New Granada, is not at all powerful. He states that he has frequently wounded birds, pigs and other animals with it without producing any marked result. The Indians, however, told him that they used a more virulent poison when they went to war, but if this be true, he was unable to obtain any of it. He has never heard them call any of their poisons by the name of corroval or vao.[2] In regard to the manner of manufacturing the varieties we refer to we have been unable to obtain as yet any information.

[1] Physiologische und Toxicologische Untersuchungen über Curare. Virchow's Archiv, Elfter Band, 1857, s. 401. See also Comptes Rendus, t. xliv., 1857, p. 507.

[2] Also Rough Notes, &c. By John C. Trautwine, C. E. Philad., 1854, p. 65.

CORROVAL. *Physical and Chemical Characters.*—The corroval when in large lumps is of a brownish black colour. Reduced to fine powder, it becomes a tawny yellow. The larger pieces have very much the appearance presented by vegetable extracts of the same colour. Its taste is intensely bitter and very persistent. The saturated aqueous infusion is of a very dark-brown almost black colour, and of neutral or exceedingly slight acid reaction. The alcoholic tincture is of a pale yellow tint. Both water and alcohol extract the active principle. The insoluble residue, viewed by the microscope, is seen to consist of vegetable cells, starch granules, and other vegetable structures, oil globules, &c. Small grains of silica are also to be observed. No parts of animals of any kind can be discovered (Fig. 1). It is very certain that these latter do not enter into the composition of corroval.

Fig. 1.



In the aqueous solution large colonies of infusoria are found, probably all of a vegetable character.

The aqueous solution mixed with blood does not retard its coagulation or alter the shape of the blood disks more than would any bland fluid of similar density. It is not at all poisonous to plants. We have inoculated tender flowers with it repeatedly without producing any effect upon them.

In order to separate the active principle from the corroval, the following processes were adopted:—

1st. Ten grains of the substance were extracted by repeated portions of boiling water, till a bitter taste was no longer afforded. The solutions were now mixed and boiled with magnesia. The whole was thrown upon a filter and the residue well washed with boiling alcohol. It was perfectly insoluble, showing, therefore, the absence of strychnia.

The filtrate was filtered repeatedly through animal charcoal, till all the bitter principle and colouring matter were absorbed. The charcoal was then treated with boiling alcohol in fresh portions till all bitterness was entirely extracted. The alcohol was then evaporated to dryness. By this process a greenish white substance, insoluble in water, was obtained. It was readily dissolved by alcohol, ether, or chloroform. It is not crystallizable. It forms salts with hydrochloric, nitric, and sulphuric acids, neither of which crystallize.

2d. The process employed in this instance was that used by Roulin and Boussingault, but modified by employing water to extract with instead of alcohol.

Ten grains of the corroval were reduced to fine powder and extracted with water, as in the first process. To the solution tannic acid was added, a voluminous flaky precipitate of a yellowish white colour was thrown down. This was well washed in a filter, to remove the tannic acid, mixed with water and heated to boiling, a few crystals of oxalic acid being added, till it was entirely dissolved. The acid liquor was next treated with magnesia in excess, and filtered. The filtrate was evaporated to dryness, and the extract thus obtained dissolved in hot alcohol. This solution evaporated to dryness furnished a substance similar to that obtained by the first process, but more highly coloured.

For the substance procured by the foregoing processes, possessing as it does all the qualities of an alkaloid, and in an eminent degree all the toxic properties of the corroval, we propose the name of *corrovalia*. We regret that we are unable, owing to the smallness of the quantity, to enter at present more fully into the chemistry of this interesting substance. From repeated observations we have, however, ascertained that it produces effects upon the animal organism precisely identical with those caused by the corroval itself, requiring, however, an infinitesimally smaller dose.

Physiological Investigations.—The action of corroval upon the animal organism is so entirely different from that of the ordinary woorara, as to indicate very strikingly its dissimilar composition. At the same time, the more obvious effects do not present any considerable variation. This is well shown from the following experiments:—

Experiment. A pigeon was inoculated near the cloaca with a little strong infusion of corroval. The bird at first exhibited no uneasiness. After the lapse of two minutes it walked a few steps, and began to show signs of discomfort. At the end of four and a half minutes it suddenly fell, flapped its wings once or twice, and died without further struggle.

Expt. A large owl was inoculated with a small fragment of corroval in the leg. Owing to the density of the tissues of the part, or to some other cause, the poison was not absorbed after twenty-five minutes had elapsed. It was therefore again introduced, in solution, under the left wing. After three minutes continuous movements of the muscles of the throat were induced. The bird staggered, let its wings fall, and appeared to stand with difficulty. About the end of the sixth minute it fell, and died without the least convulsive movement. The pupils were enormously dilated.

Expt. A mouse was pricked with a knife charged with a solution of corroval. It fell dead in three and a half minutes, without the slightest spasm.

Expt. Under the skin of a large frog a few drops of a strong solution of corroval were introduced. The animal remained, apparently, unaffected for twenty-five minutes; at the end of this period paralysis of the voluntary muscles commenced. When quietly laid upon the back, and the extremities stretched out, no effort was made to assume another position; when irritated, however, the extremities were withdrawn. The frog was entirely dead in forty-eight minutes—*i. e.* exhibited no motion of any kind to ordinary stimulus.

These experiments are sufficient to show the general effect and virulence of the corroval. It is perceived that, so far as these points are concerned, its action is very similar to that of the strongest woorara. There is no

tetanic spasm, a fact which sufficiently proves the absence of strychnia. As we shall presently show, however, when the action of the corroval is more physiologically considered, many important points of difference between it and the ordinary woorara will be found to exist.

Action on the Heart.—The woorara hitherto used by experimenters was found, as we have already seen, to exercise little or no direct influence on the heart. This organ continued to beat in all animals for a considerable period, and, even after it had entirely stopped, it could be made to resume its actions by artificial respiration. The action of the corroval is in this respect directly antagonistic, as will be perceived from the following experiments:—

Expt. A small frog was poisoned with corroval by inserting a minute piece of the substance under the skin of the back. The chest was then opened, so as to show more distinctly the action of the heart. During the third minute after the insertion of the corroval the heart beat forty-five times, and very irregularly. For the fourth minute the pulsations were but thirty. During the fifth minute the ventricle acted in a very singular manner, small portions of its tissue being apparently paralyzed, and bulging out, whilst the rest was contracted. The pulsations were but eighteen. In five and a half minutes from the inoculation the ventricle had entirely ceased beating, and had contracted to a very small bulk. It was hard and rigid, and of a pale-red colour, showing the entire absence of blood both from its tissue and cavity. The auricles continued to act for two minutes longer, when they also ceased. Instead of being contracted, the auricles were rather dilated. Galvanism was applied to the heart, without having the slightest effect in exciting it to action. The lungs or air-sacs were perfectly collapsed.

During the whole of this period the voluntary muscles were active. The frog struggled violently to escape, and finally succeeded in leaping to the floor. It remained active for twenty minutes. The pupils, which, at the time the heart ceased to act, were contracted, now became dilated, and all voluntary movements were abolished.

Expt. A pigeon was inoculated with a little strong aqueous solution of corroval. It fell dead in five and a half minutes, without convulsive action. The pupils were enormously dilated. The chest was immediately opened, and the heart was found to have ceased pulsating. Under the influence of a powerful galvanic current a few fibres contracted two or three times. It was incapable of further excitation. The ventricles were somewhat corrugated, and the auricles dilated. The peristaltic action of the intestines was readily excited by galvanism for about half an hour.

Expt. A rabbit was inoculated in the leg with a little strong infusion of corroval. In three minutes the animal exhibited great uneasiness, and constantly moved the jaws, as if chewing something. In six and a half minutes it fell dead, without the least spasm of any kind. The pupils were largely dilated. The chest was immediately opened, and the heart was found to have ceased pulsating. The ventricles were small and empty; the auricle contained a quantity of dark fluid blood. A single ventricular contraction was induced by galvanism.

Expt. The crural nerves of a very large frog were isolated, and a ligature placed under them and tied tightly so as to include all the tissues but the nerves. A large quantity of the aqueous solution of corroval was then injected under the skin of both legs. The chest was then opened, so as to show the movements of the heart. These did not seem to be disturbed, except by the impediment caused to the circulation by the ligature. After ten minutes the pulsations were forty-five per minute. At the end of half an hour the heart was still active, beating forty-eight times per minute. The ligature was now removed. The heart almost immediately began to exhibit the ordinary signs of the action of the corroval—viz., the partial paralysis and irregular contractions which it occasions - and in

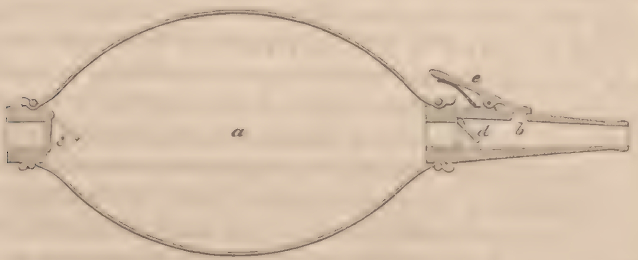
six and a half minutes the ventricle had entirely ceased to act. The auricles pulsated for two and a half minutes longer. No contractions could be induced by galvanism. Dilatation of the pupils ensued in twenty-five minutes, and all voluntary movements ceased.

From the foregoing experiments relative to the action of corroval upon the heart, which have been frequently repeated, with uniform results, we arrive at the conclusion that it acts directly upon this organ by being carried to it through the circulation. It is well known that in cold-blooded animals the respiration may entirely cease, and the heart nevertheless continue its action for a considerable period afterwards. These results, indeed, follow the poisoning of such animals by the ordinary woorara; and, as Brodie, Waterton, and numerous other experimenters, have shown, if the respiration be continued artificially in warm-blooded animals poisoned with this substance, life may be preserved; and even after the heart has ceased to act, it will again resume its movements under this influence. The discontinuance of the function of the heart through the action of the corroval must therefore be regarded as a primary effect, in no degree dependent upon the respiratory process, but due, as we have already stated, to the direct influence of the poison upon the heart itself. In order, however, to place the matter beyond doubt, the following experiment was instituted:—

Expt. The trachea of a cat was opened, and a tube introduced, to serve for the attachment of an apparatus for conducting artificial respiration.[1] A quantity of strong infusion of corroval was then injected under the skin of the flank, and the chest immediately opened. Artificial respiration was then instituted. The heart was actively pulsating. In a few moments its operation became irregular, and at length ceased entirely, seven and a half minutes after the introduction of the poison. The pupils, which at first were contracted, gradually enlarged to their fullest extent.

[1] The apparatus we have devised for the purpose stated, and of which a figure is annexed, has been found to answer very admirably, and can be much more easily

Fig. 2.



managed than the ordinary bellows. An India-rubber bag (a) has openings in both ends, into which two brass tubes are fixed, provided with valves (c, d). The tube b is attached to a tube of India-rubber, which, by a nozzle and stopcock, is inserted into the trachea. When the bag is squeezed, the valve c is closed, and the valve d opening, the air passes into the lungs. On removing the pressure, and raising the valve e, the air escapes from the lungs through it, the valve c opens, the valve d closes, and the bag again becomes filled.

The instrument was made for us by Messrs. J. W. Queen & Co., 924 Chestnut St.

The independence of the heart in relation to the respiratory process is thus fully shown, and one of the main points of difference between the action of the corroval and that of the woorara indicated. It is perhaps useless to bring forward further illustrations in support of the facts we have stated; but the following experiment is so apposite and conclusive, that we cannot refrain from adducing it:—

Expt. A young alligator, about a foot in length, was properly arranged, and the chest opened. The heart was beating thirty-six times per minute. A little solution of corroval was next introduced under the skin. The pulsations of the heart, five minutes afterwards, were thirty-four per minute. The respiratory actions were vigorous, and perfectly effectual. After twelve minutes the action of the heart commenced to be irregular, and the pulsations had fallen in number to twenty-eight per minute. The rhythm of the auricles with the ventricle was entirely reversed, and the former was very curiously corrugated. The heart ceased acting (both auricles and ventricle) seventeen minutes after the inoculation. The left auricle was of a pale-red colour, the right was black, the ventricle was pale and contracted. The heart stopped immediately after vigorous and long-continued respiratory movements. The lungs were well filled with air, and respiration was actively continued for sixteen minutes after the heart had ceased to pulsate. The pupils, which for a few minutes before the heart became affected were contracted to mere lines, were now dilated to a great extent, and all voluntary movements ceased.

From the foregoing experiments, we do not see how any other conclusion than the one we have stated can be adopted—viz., that the discontinuance of the heart's action is a primary result, and not due to the disturbance of any other function. Whether we regard the cause of its motion as being due to muscular irritability or to the ganglia found throughout its tissue, we cannot avoid the inference that both are powerfully influenced through the action of the corroval. In the experiment last stated we have seen that the rhythm of the heart was greatly disturbed, and that it continued to pulsate in the most irregular manner. We might adduce numerous other observations to the same effect. All this brings us to the conclusion that the ganglia are primarily affected, especially as from the contraction of the pupils and the cessation of the capillary circulation, to which we shall presently allude, we are led to infer the paralysis of the sympathetic nerves. No doubt, however, can exist that the muscular irritability of the heart is also completely destroyed, for no irritation, not even that of the strongest galvanic current, can re-excite its pulsations a minute after they have ceased; and even before the lapse of this short period we can obtain but one or two feeble manifestations of the force which once caused its throbbings.

We have as yet said nothing relative to the action of the corroval upon the *lymph hearts* of frogs. Without stating the experiments in full, we may say that, from frequent observations, we have convinced ourselves that under the influence of this agent they cease to pulsate in from twenty to thirty minutes after its introduction into the circulation.

We may here refer to the influence of the corroval over the *capillary circulation.* We have uniformly found it to be arrested one or two minutes before the ventricle stopped acting. We consider this to be due to paralysis of the sympathetic nerves.

Whilst viewing the web of a frog's foot, in order especially to satisfy ourselves relative to the above point, we have never seen any alteration in the size, colour, form, or number of the red or white corpuscles. We have already, however, stated our views upon this subject.

The action of the corroval upon the *nervous system*, though in one or two respects similar to that of the ordinary woorara, is, we think, in others materially different. The latter destroys all voluntary and reflex movements immediately; it acts exclusively on the motor nerves, leaving the sensitive nerves unaffected, as Bernard has satisfactorily shown. As we have demonstrated, the first action of the corroval is directly upon the heart, and hence we have one important point of difference in the effects of the two poisons. In considering the action of this substance upon the nervous system, we shall indicate other points of dissimilarity.

1. *Influence of Corroval upon the Voluntary and Reflex Movements.*—*Expt.* A large frog was inoculated with corroval under the skin of the back. The heart ceased pulsating in seven and a half minutes. The frog continued active for twenty minutes after the insertion of the poison, and at the end of twenty-five minutes all voluntary movements had ceased, paralysis first occurring in the anterior extremities. If now an extremity was irritated, it was immediately withdrawn, and galvanism applied to one foot excited movements in all the others. This condition remained for forty-five minutes after the introduction of the corroval, when it was changed, and reflex movements could only be excited in the nictitating membrane. In one hour and five minutes all reflex movements were lost.

Expt. A young alligator was inoculated with corroval under the skin of the flank. The heart ceased acting in seventeen minutes, and in thirty-five minutes all voluntary movements were abolished, the anterior extremities first losing the power of motion. Upon pinching the tail, violent reflex motions were excited in all parts of the body, including the lungs, and strong respiratory movements were produced. They were readily excited for more than an hour and a half after the stoppage of the heart.

Numerous other experiments could be adduced to the effect above indicated—viz., that in cold-blooded animals the voluntary and reflex movements remain for a considerable period after the cessation of the heart's action, and consequently much longer than after poisoning with the ordinary woorara. At first sight it appeared to us that the abolition of these manifestations of the integrity of the brain and spinal cord, which eventually occurred, was due to the direct action of the corroval; but after the institution of other experiments, and a fuller consideration of the subject, we have arrived at a very different conclusion. In order to ascertain the effect upon the brain and spinal cord of the cessation of the heart's action, or, what amounts to the same thing, the prevention of the passage of the blood to or from them, we performed the following experiment:—

Expt. The chest of a large frog was opened, and a ligature placed around the vessels at the base of the heart. All voluntary movements ceased in twenty-five minutes; and at the end of fifty-five minutes no reflex actions could be excited in any part of the body. The sciatic nerve of the left posterior extremity was exposed, and, on being irritated, strong contractions were produced in the muscles of the leg. This condition was present at the end of two and a half hours.

The experiment was frequently repeated, with uniform results. The voluntary movements always ceased in from twenty-five to thirty-five minutes, and the reflex in from fifty minutes to an hour and a quarter, after the ligation of the vessels. We consequently feel warranted in concluding that the cessation of these actions in animals poisoned with corroval is an indirect effect resulting from the cessation of the function of the heart, and therefore not due to any specific effect upon the brain or spinal cord.

2. *Action upon the Nerves and Muscles.*—The woorara, as experimented with by Bernard, Kölliker, and others, was found to immediately destroy the excitability of the nerves, leaving that of the muscles unaffected, or perhaps augmented. We have not found this to be the case with the corroval, as the following experiments will show:—

Expt. A large frog was inoculated with a little strong solution of corroval. The movements of the heart were arrested in seven minutes. Voluntary motion ceased in about twenty-five minutes, and the reflex in about an hour, after the introduction of the poison. The sciatic nerves of both posterior extremities were now exposed. Upon gently pinching either of them, strong contractions were produced in the muscles of the corresponding leg. They remained excitable to galvanism for an hour longer. The muscles were irritable fifteen minutes after excitability was lost in the nerves.

Expt. A cat was inoculated with corroval. Death followed in about five minutes. The sciatic nerve of the right leg was exposed, and, on irritating it, strong contractions were produced in the muscles of the extremity. The nerve continued irritable to galvanism for twenty-six minutes after death, the muscles for thirty-five minutes.

Expt. A pigeon was killed with corroval, death ensuing four minutes after the introduction of the poison. The sciatic nerve was irritable for seventeen minutes subsequently. The muscles retained their irritability for twenty-two minutes.

From these experiments we see that nervous excitability remains for a longer period than in cases of poisoning with woorara. This function is nevertheless affected by the corroval, for, as we have seen, it remains much longer present in animals whose circulation has been arrested by ligature of the large vessels. Consequently the mere deprivation of oxygenated blood, or the retention of that which is not decarbonized, cannot be the cause of its abolition, and we must therefore ascribe it to the direct action of the poison.

We also perceive that the muscular irritability was lost very soon after that of the nerves, and consequently we have here another point of difference with the woorara. It may perhaps be thought, by those who disbelieve in direct muscular irritability, that the reason why the muscles appeared irritable after the loss of excitability in the nerves was due to another cause—viz., the retention of this faculty in the minute ramifications of the nerves after its loss in the larger trunks. In relation to this point, we think we can show that the corroval, like the ordinary woorara, causes the death of the nerves from the periphery to the centre, and, consequently, that the minute ramifications lose their vitality before the larger trunks. In illustration we subjoin the following experiment:—

Expt. A few drops of the strong infusion of corroval were introduced under the skin of the back of a large frog, the sciatic nerve of the left side having been

previously cut. The heart ceased to act in eight minutes—voluntary and reflex movements ceased respectively in thirty and fifty-five minutes. The sciatic nerve of both sides were excitable, the left in a less degree than the right. After the lapse of an hour and a half, the left nerve had entirely lost its irritability, whilst the right was still excitable, and remained so for twenty minutes longer.

With strychnia, however, the effect is far different, this substance destroying the nervous excitability from the centre to the periphery, as the following experiment shows.

Expt. Under the skin of a large frog, whose left sciatic nerve was previously divided, a few drops of a strong solution of strychnia were introduced. Tetanic spasms ensued in two minutes. After forty-five minutes the nerves were irritated by galvanism. That of the left side, which had been cut, responded energetically, whilst no motions could be produced through the uncut nerve. The former remained excitable for two hours later. Muscular irritability was strong in both legs. The experiment was not further pursued.

We infer from the foregoing experiments that the irritability of the muscles is a faculty entirely distinct from the irritability of the nerves, and that accordingly it may be present after the entire abolition of the latter. The fact that the corroval destroys the excitability of the nerves from the periphery to the centre, acting first upon the small branches, and subsequently upon the larger trunks, is, we think, abundantly shown. Hence the contractility exhibited by the muscles on being galvanically irritated could not be due to excitability remaining in the minute nervous radicles.

With reference to the effect of woorara upon the sensory and motor nerves, it was found by Bernard and Kölliker that the latter first lost their vitality, the former not being directly affected. By confining the action of the poison to certain portions of the body, Bernard obtained movements in a non-infected limb by irritating one that was fully poisoned. Hence he proves that the woorara does not affect the integrity of the sensory nerves. We have performed his experiments frequently, substituting corroval for woorara, without obtaining his result. They are as follows :—

Expt. The vessels of the left posterior extremity of a medium sized frog were ligated, and all the tissues, with the exception of the sciatic nerve, divided. The limb was consequently only connected with the body through the medium of the nerve. The animal was then inoculated with corroval high up in the back. The movements of the heart were arrested in six minutes—voluntary and reflex movements ceased about the usual time. On irritating either of the anterior extremities, or the posterior leg which was not cut, no motions were excited in the left posterior extremity, showing, therefore, that sensation was entirely destroyed by the corroval. The irritability of the muscles subjected to the influence of poison was lost in one hour and fifty minutes after the inoculation, whilst it was present in the non-poisoned limb sixteen hours afterwards. The animal was not further observed.

Expt. The sacrum of a large frog was carefully removed, and the crural nerves isolated by passing a ligature around the body so as to include all the tissues but the nerves in question. This was tightly drawn and tied so as effectually to prevent the circulation of the blood in the posterior extremities. The frog was now inoculated with a solution of corroval in the manner last stated. The heart ceased to act in six and three-quarter minutes—voluntary movements were abolished in thirty minutes, and all reflex actions were lost in fifty-three minutes after the introduction of the poison. Strong galvanic irritation was now

applied to the anterior extremities, and although muscular contractions were induced in them, there were no reflex movements in the posterior extremities. The sensory nerves had therefore lost their faculty of conveying impressions. Muscular irritability was extinct in all the anterior portions of the body at the end of two and a quarter hours. The muscles of the posterior extremities retained their irritability for twenty-two hours. The experiment was not further continued.

From these experiments it is perceived that the corroval, unlike the woorara, destroys sensation, and that so far from augmenting the irritability of the muscles, this faculty is also annihilated.

Bernard found that in animals poisoned with woorara, the muscles were red as if they contained a considerable quantity of blood. In all cases of corrovalic intoxication the reverse is the fact, provided, of course, that the circulation has not been mechanically impeded by ligatures, &c.

Absorption of Corroval.—Corroval is readily absorbed from the mucous membrane of the stomach, and from the external surface of the skin of frogs. The following experiments are cited in illustration of this point:—

Expt. Ten drops of the strong solution of corroval were placed in the stomach of a large frog. The chest was then opened. The heart was pulsating 50 times per minute; in a minute or two afterwards, the contractions of the ventricle became very irregular, the partial paralysis was present, and it ceased to act in five minutes after the introduction of the poison. The auricle stopped two and a half minutes subsequently. Slight convulsions of a clonic character now appeared in the posterior extremities, and lasted for a few minutes. The ordinary symptoms of corrovalic intoxication then ensued in regular order.

We mention it as a singular circumstance, that in all cases in which we have given the corroval internally, there were convulsive movements of the posterior extremities as above, whilst we have never seen them in frogs where it was introduced directly into the circulation.

Expt. Ten drops of the strong solution of corroval (twenty grains to the ounce) were placed upon the back of a large frog. After the lapse of fifteen minutes the chest was opened. The heart was still pulsating actively. After ten additional minutes five more drops were placed upon the back—in a short time it began to act, and thirty-five minutes after the first introduction of the poison the heart ceased. The other consequences followed in due succession.

We deem it unnecessary to enter more fully at this time into the discussion of the questions connected with the absorption of the poison, or to bring forward other experiments. They will be considered more at length under another division of our subject.

From the foregoing experiments and observations in relation to the corroval, we deduce in the main the following conclusions:—

1st. That it differs essentially from any variety of woorara hitherto described, both in its chemical constitution and physiological effects.

2d. That it acts primarily upon the heart, through the medium of the blood, producing an arrest of the action of this organ.

3d. That the annihilation of voluntary and reflex movements is a secondary result of its action, depending primarily upon the discontinuance of the function of the heart.

4th. That it acts upon the nerves from the periphery to the centre, and abolishes both the sensory and motor functions.

5th. That it destroys muscular irritability.

6th. That it paralyzes the sympathetic nerve, this being one of its primary effects.

7th. That it is absorbed both from the intestinal canal and skin of frogs.

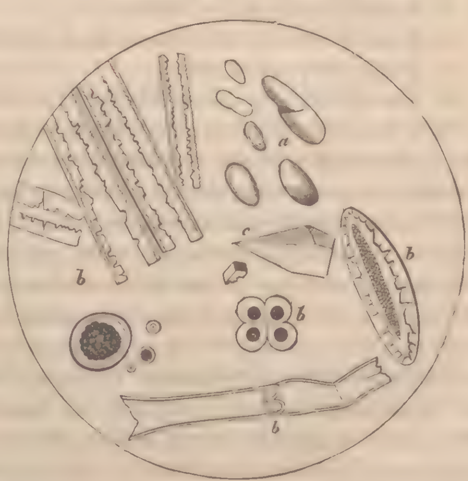
8th. That its poisonous qualities are due to an alkaloid hitherto undescribed.

Vao or Bao.—The variety of arrow-poison of which this portion of our paper treats is, without doubt, a different material from the ordinary woorara used in Europe. At first we were disposed to regard the vao as a weak specimen of the same material which M. Bernard, Kölliker, and others have studied; but a long and patient investigation of its properties and physiological reactions has forced us to the conclusion that vao poison, although it presents some points of resemblance to the arrow-poison of Waterton, De la Condamine, and the later observers, is essentially a distinct and different substance. Indeed it is by no means unlikely that the various tribes of South America employ different but allied agents to furnish the arrow-poison whose use seems to be so general in that part of the world, and we are surprised that no specimens of the varieties before us have as yet found their way into the hands of European physiologists.

We shall now proceed to consider in order the physical, chemical, and physiological characteristics of vao.

Physical and Chemical Characters.—The vao in our possession is a dark-brown extract, perfectly dry and hard, and unaffected by exposure to the air. It is partially soluble in water and alcohol. The insoluble portion consists of a white or light gray deposit, of a shred-like and flocculent appearance. Examined under the microscope, this is found to be principally amorphous matter with a considerable admixture of starch-cells (Fig. 3, *a*), and various forms of entire or broken cells, all of vegetable origin (*b*). A few broken crystals are also found (*c*), but no indications whatever of the

Fig. 3.



presence of any relics of animal tissues, such as we should naturally look for were snake-heads and ants employed to make up this deadly material. The solutions of vao are of a tawny yellow hue, and are feebly acid.

In the chemical examination of vao, the same processes were employed as were resorted to in analyzing corroval, and an alkaloid was obtained, which differed in no essential physical or chemical character from that of corroval. When, however, equal quantities of corroval and vao were analyzed, the latter material yielded the smaller amount of alkaloid. The result of the physiological comparison of the two substances extracted from the poisons in question will be found elsewhere.

Before proceeding to study the effect of vao upon the tissues and organs, it will be well to present a general view of the symptoms and appearances offered to the eye by an animal poisoned with it, reserving their interpretation for after consideration.

Expt.—A morsel of vao was introduced under the skin of the belly of a large frog. No remarkable symptoms were noticed during the first twenty-seven minutes. The frog leapt about as usual, making violent efforts to escape from the receiver. At the close of this time his fore legs were weak. Twenty minutes later the hind legs were also weak, and although he remained in any unusual posture in which he might be placed, he still retained the power to move, apparently at will, and when irritated. Fifteen minutes later all volitional control had departed in the extremities, although he retained the power to lift his head, and exhibited reflex motions of one leg when the other was irritated. At the close of the next hour the reflex acts ceased, the eyelids being the last muscular part which responded by reflex acts to external applications. Three hours and fifty-seven minutes elapsed between the inoculation of the vao and the loss of motor power in the lids. It is also to be observed that the frog continued to use the respiratory muscles of the lower jaw, and more rarely of the flanks, some time after he had lost all voluntary control of the extremities.

The order of externally visible phenomena is therefore as follows:—

1. Loss of power in the fore legs.
2. Loss of power in the hind legs.
3. Loss of reflex manifestations in the extremities.
4. Respiratory efforts cease.
5. The eyelids are no longer irritable, and do not close when touched.

In a few cases the frogs also exhibited convulsive motions, the hind legs being extended with considerable force, but not remaining rigid in this posture, as occurs when strychnia has been used.

When a warm-blooded animal, as a rabbit, is the subject of the action of vao, no marked symptom is observable until the head begins to droop and the animal crouches on his belly at the close of about twenty minutes. Before this occurs there is sometimes noticed a chewing movement of the jaws and some gritting of the teeth, a symptom which is often marked in rabbits poisoned with tincture of veratrum viride. At the close of fifteen or twenty minutes, as we have said, the head begins to sink, is jerked up, falls lower, is again jerked up, and at last is no longer lifted. Meanwhile the animal falls over on his side. The respiration becomes weaker and

less frequent. The heart beats more slowly. Slight convulsive motions of the ears and hind legs occur. The pupil, previously contracted, dilates, and in some cases the muscles of the skin are affected with a general movement. At last the respiration ceases, and the lids are no longer irritable. Meanwhile the heart is still acting feebly, and the temperature has fallen. After death the pupil contracts, and post-mortem rigour succeeds at an interval of from one to five hours.

The time required to destroy a rabbit is usually about half an hour or forty minutes, when the poison is introduced under the skin. Pigeons similarly treated die within fifteen minutes.

It will be seen from these statements that vao poison acts less rapidly than corroval, or the ordinary woorara of European observers. And this was even more manifest in the case of a cat whose symptoms differed very remarkably from those already described.

Expt. A large black cat received in the thigh a lancet-point charged with dried vao. After two minutes it was withdrawn, and found to have lost most of its poison. During thirteen minutes the animal showed no marked signs of the action of the vao, except a tendency to rest couched on her breast, and some indisposition to move about. Two minutes later she rose to her feet and made the same motions of swallowing and chewing which we have noticed in the rabbit. These proved to be the first symptoms of a violent vomiting which followed almost immediately. This action accomplished, the cat again rested on her belly, her head drooping as before, until after eleven minutes had passed, the chewing movements began again, and another violent attack of vomiting brought her to her feet. On this occasion only a little mucus was rejected. The head again sunk as she lay down, the respiration became short and quick, and the heart beat more slowly. Forty minutes after the vao was used she could still raise her head, and the eyes followed the motions of a candle passed to and fro in front of them. In the next five minutes the head fell on one side, and the body rolled over a minute later, the pupils dilating to their utmost extent. Fifty-five minutes after the vao was given the cat died in the most frightful general convulsions, with foaming at the mouth, vomiting, and ejection of urine and feces.

The difference between the external symptoms in this animal and the rabbit is as great as the effect produced on one and the same species of animal by two dissimilar poisons.

M. Bernard has never seen vomiting caused by woorara, but we cannot find that he has experimented with cats.[1] Virchow had already noted the fact that the cat is subject to convulsions when poisoned with woorara, and in this respect the vao poison resembles it. Cats are, however, so liable to convulsions that almost all poisons produce them, and very trivial causes will bring them on in kittens apparently in health. Thus we have seen a cat frightened into wild epileptiform convulsions.

Absorption.—In this connection it is still to be held in mind that the

[1] The chewing movement which we have described as preceding the act of emesis in the cat, was also noted in nearly all of the warm-blooded animals poisoned with either corroval or vao. In one of them, a pigeon, vomiting took place. It is possible that the peculiar movements alluded to may be indicative of the existence of nausea which does not reach the actual climax of vomiting.

variety of woorara poison which we have now in view is far less active than the woorara examined by Bernard and Kölliker, and even less so than the corroval of which a portion of our paper treats.

The phenomena which announce the absorption of the vao are therefore slower in appearing, and have sometimes to be awaited a considerable time. The actual length of time required for absorption to occur is, however, of less moment than the facts relative to the absorbing power of the various tissues with which the poison may be placed in contact, and the exterior circumstances which seem to be influential in determining the rate of absorption.

Most of our experiments have been made upon frogs. We shall detail the results with reference to the various tissues.

Areolar Tissues.—When a morsel of vao was placed under the skin of a frog death inevitably ensued, whether the animal was left in dry or moist air, or in water, and no important difference was observable in these several cases, save that when a solution was employed the death was more rapid than when the solid poison was used. Thus, a frog of middle size received under the skin of his back a morsel of vao. In four hours all motion, voluntary and reflex, had departed. A second frog, of rather larger size, having received in his subcuticular sac the same amount of vao dissolved in water, perished in forty minutes.

The same general rule applies to those warm-blooded animals upon whom the poison was tried. An equal amount of vao being placed under the skin in two rabbits of about the same size, the one which received the vao in solution perished in eighteen minutes, while the other lived for half an hour.

Absorption by the Skin.—Vao, like woorara, is best absorbed by the skin of the frog, when the skin is comparatively dry, a fact which is due to M. Bernard, and which he conceives to be owing to the constant exhalation of a viscous and protective mucus, which is abundant when the frog is in, or just removed from the water, and which is scarcely observable when the frog has been long out of that element. The following experiments sufficiently illustrate these facts with reference to vao.

Expt.—A large frog which had been kept under a receiver open at top during several days, was found to have a skin much less lubricated than that of a frog kept in water. The skin at the middle of the back was cleaned with a piece of cotton wadding, and a small portion of a paste composed of vao was put upon the spot thus deprived of its mucus. The frog being replaced in the receiver, at the end of seven and a half hours all motion was lost.

Expt.—A frog of smaller size was so imprisoned in a net of wire that he remained with about half of his body under water. Upon his back was put a smaller amount of vao paste than was used for the last frog, but the situation chosen was the same, no attempt being made to rub off the mucus. Although the vao was twice renewed within forty-eight hours, no accident resulted to the animal, nor was he to appearance in any way affected by it.

That, however, the amount of absorbing surface exposed to the action of the poison may modify the result very materially, was seen in the following experiments :—

Expt. A small but very active frog, which had just been removed from the water, had one leg imprisoned in a piece of thin caoutchouc tubing, which was

well filled with cotton saturated with an aqueous solution of vao—one grain to the ounce of distilled water—a morsel of the solid poison was also thrown into the tube, and the open end closed with slight pressure around the leg, above the knee. At the end of four hours and forty-five minutes, reflex motions were no longer to be excited by galvanism.

Expt. The last described experiment was repeated with the single variation of placing the frog half under water, taking care to keep out of the water the leg which was in the tube and surrounded by poison. At the close of five hours no effect was visible. At the end of twenty-five hours the frog was sluggish—three and a half hours later all movement, reflex and voluntary, was over.

These two experiments, with others of a like character, seem to show that when a large amount of surface is exposed to vao in solution, and but half of the remainder of the body placed in water, absorption may occur; the same result being attained in a far shorter period when one leg being kept moist with vao, the rest of the body is exposed to the desiccating influence of the atmosphere.

Now that the production of mucus does protect the frog to some extent cannot be doubted, and has been proved by M. Bernard with his usual experimental skill. It will be seen, however, from the next set of experiments, that the amount of moisture in the system of the frog has much to do with his power to absorb the vao in solution, so that it is not only the exudation of mucus, but also the excess of watery supply which enfeebles the absorptive process. When the frog is dried more or less by long exposure to the air, his body eagerly takes up the moisture which is presented to any part of the surface. When, on the other hand, his body is thoroughly moistened, and the supply of water is in contact with the larger part of his surface, the power to absorb an aqueous fluid of a higher specific gravity than water from any one part of the surface is considerably lessened. Of course the presence of water is essential to the production of the viscous mucus, which is supposed to be the means of protecting the wetted frog, but it is also probable that the varying supply of water regulates the rate of absorption of aqueous solutions placed in contact with a part of the skin, or, as we shall now show, in the interior of the digestive canal.

Absorption from the Digestive Canal.—Expt. A small frog received in his stomach thirty drops of a solution of vao, one grain to the ounce of water. The dose was given through a glass tube, whose edges were carefully rounded that the mucous membrane might not be wounded. None of the poison escaped. The frog was placed on a damp cloth in a receiver containing a wetted sponge. At the end of nineteen hours and fifteen minutes he was found to be inert and sluggish, though still able to raise himself when suspended by one leg. In twenty-two hours longer he was unable so to lift himself. Seven hours later all motion had departed—the bared muscles were feebly irritable to galvanic stimulus, and the heart beat in successive minutes 2, 2, 2.

Expt. A second frog which had received the same dose in the same way, and at the same time, and which had also been placed in like circumstances, died during the ensuing night.

Expt. A small frog received thirty drops of the same solution and was at once placed in water. At the end of four days he was perfectly well.

Expt. Two small frogs received each of them thirty drops in the stomach,

and were placed together in water. No. 1 lost all reflex and voluntary motions at the close of twenty-four hours. On examination no sufficient cause could be found to explain his early death.—No. 2 was well and active after five days.

Expt. A small frog received in his mouth a morsel of vao, which he twice rejected—it was finally placed far back and to one side. He was then left upon paper, that the poison might be seen if again rejected; a large receiver was then placed over him and he was left to himself at 12 M. He died during the ensuing night.

It follows from these experiments that vao in the dose here stated is poisonous to frogs when placed in the mouth or when directly carried into the stomach. It will also be observed that the frogs which, after receiving this dose, were placed in water, suffered but little—one out of three perishing within four days, while frogs of the same size who were treated in like manner, except that they were confined in an atmosphere more or less dry, one and all suffered from the poison. Still, as it was possible that the frogs which, being placed in water, survived, might have rejected the poison, or diluted it largely and frequently by swallowing the water in which they were placed, it became necessary to test this negative result.

Expt. Accordingly a frog of middle size received in his stomach by a tube thirty drops of the one-grain solution. Three wire ligatures were next carried through the skin of the upper and lower jaw, at a little distance from the lips, and firmly twisted, so that no water could easily enter or leave the mouth. Thus prepared, the frog was suspended in water, his head alone remaining above the surface. At the close of the second day he was rather sluggish, but on being released and allowed to remain at liberty for a time he did not seem to have been materially affected. Replaced in the water, he was observed at intervals up to the close of the fourth day, when, as he seemed in no wise the worse for the poison, he was set free, and the observation ceased. It is not, therefore, direct dilution with water which renders the ingested poison so harmless to frogs kept in that fluid.

The power of different parts of the intestinal canal to absorb the vao poison was also the subject of numerous experimental tests. The stomach was the organ first essayed, and to try its absorbent powers, we utilized a fact in the physiology of the frog which has been known to one of the authors of this paper for some time, but which we do not find elsewhere referred to. Under certain circumstances, a detailed account of which will be found in a note, the frog can be made to evert first the œsophagus and then the stomach, so that it is literally turned inside out, and projects from the mouth, its internal or mucous coat being exposed to the air.[1]

[1] Some time since, one of us, Dr. Mitchell, observed that when an irritating substance, such as tinct. veratrum viride, is poured into the mouth of a frog, the animal sometimes, by a sudden effort, everts the œsophagus, and then the stomach, so that the mucous surface of the latter organ projects from the mouth. If the frog be left to himself, he remains rather sluggish for a time, and finally returns the viscera to their usual places apparently none the worse for this extraordinary performance. Suspecting that the pressure upon the abdominal walls, which cannot well be avoided when holding a frog, might have been influential in forcing the stomach out at the mouth, an attempt was made to produce the result in this manner alone, but without success. Since these facts were observed, Dr. James Darrach informs us that he has twice seen frogs who had thus everted the viscera while in water and at perfect liberty. At all events, it is very difficult by any manage-

Expt. A large frog thus prepared received on his everted stomach a morsel of vao made into a paste with a little water. A portion of the mucous membrane of the œsophagus at some distance was then secured in the grasp of a Liston forceps, and the shank of the handle slipped over a nail which was driven into the table. One of the fore feet of the frog was next secured by a wire so that he could not return the viscera to the belly again. A morsel of vao being placed on the surface of the stomach, he ceased to move in ten hours.

Expt. In this case the lower jaw-bone was divided on both sides, so that he would be unable to aid himself by forcing the stomach into place again. Notwithstanding this precaution, the frog reverted his stomach after the lapse of some hours, but not before he had exhibited indubitable signs of being poisoned. He died within twenty-four hours of the administration of the vao.

Expt. Two frogs were similarly treated, except that no vao was placed upon the everted organ, and that in one case the stomach was transfixed with a needle and thus retained in its strange position during twenty-four hours. The other frog restored the viscera to their places within two hours. When the needle was withdrawn from the stomach of the first frog, he made no immediate effort to replace his organs. Being put in water he seemed sluggish, but on examination next day proved to have succeeded in re-arranging his disturbed anatomy. Both frogs were well three days later.

In these experiments the stomachal mucous membrane was rather dry, and the whole organ much congested. The effect was less rapid than in the following experiment, where no doubt the local circulation was less interfered with.

Expt. The abdomen of a large frog being opened, the stomach was drawn out, and a ligature tied around the pyloric extremity. A morsel of vao was next slipped into the stomach through a slit in the œsophagus, and ligatures placed about the cardiac end of the viscus, and about the œsophagus above the wounded part, which was carefully excised. The vao acted fatally within two hours, an unusually sudden effect to be produced by this mode of using it. Lest a minute portion of the vao might have been left upon the wounded œsophagus, the experiment was repeated, with the variation of using a small tube through which the vao was carried into the stomach without opening the œsophagus, which was, however, tied just above the stomach. Poisoning took place in this experiment within five and a half hours. The frogs used had been just removed from water, and were afterwards left under bell-glasses, as usual. Still, the effect was rapid. On examining the stomachs after death, we could not see that the ligatures had cut the internal coat, although they undoubtedly did bruise it, and perhaps imperceptibly tore its delicate surface.

Absorption by the Mouth and Œsophagus.—Expt. The belly of a frog of middle size having been opened, and the œsophagus tied, the wound was closed, and a morsel of vao placed in the mouth. At the close of eighteen and a half hours he was active and well; a little jelly-like mucus could be seen at the back of his throat, tinged with the dissolved vao. Five and a half hours later his fore legs were feeble, and he could no longer lift himself by one leg when held suspended by it. Twenty hours later he was found devoid of motion in his limbs. The nerves were no longer irritable, but the heart beat three, three, three in successive minutes.

Expt. A small frog was poisoned by the subcutaneous administration of the

ment, short of the means first mentioned, to obtain this result, without the co-operation of the frog. It is probably a mode of vomiting, and a normal physiological act. For purposes of experiment, such as those described in the text, the stomach may be everted by firmly pressing the belly with one hand, and with the other passing into the stomach a thermometer with a bulb larger than the stem. As this is withdrawn, partial eversion of the organs occurs, and may be made complete by a little manipulation with a pair of forceps carefully used.

vao, which was still found after death, dissolved, in the buccal mucus of the subject of the last experiment. The mucus, therefore, does not alter the poison.

Absorption by the rectum takes place both in frogs and higher animals with considerable ease.

Expt. A morsel of vao, placed in the rectum of a small frog, produced death within thirty-nine hours.

Expt. A very large frog was opened, and the rectum divided. A morsel of vao was passed through a tube into the lower segment of the rectum, and ligatures were cast about the cut ends of the intestine, which was finally returned to the abdomen, and the wound sewed up. The frog was left under a bell-glass containing a damp sponge. He was not observed until twelve hours had elapsed, when he was found dead; the heart not beating, and the muscles scarcely irritable by galvanic stimulus. No trace of the poison could be seen in the rectum, except a small white shred, like the undissolved portion of vao which forms the sediment in its aqueous solutions.

Expt. A small rabbit, into whose rectum was thrown an injection of vao containing about one-eighth of a grain, perished within one hour, notwithstanding that he had rejected a large part of the poison.

The vao poison is, therefore, readily absorbed by the rectal mucous membrane, as was also found by other observers to be the case in their own experiments. It follows, as a general deduction from our researches upon the absorbing power of the various tissues for vao poison, that the rectum, stomach, and mouth in the frog are all capable of admitting the poison to the system through their mucous surfaces; absorption by the skin or stomach being governed, as to its rapidity, by the needs of the system for aqueous fluid.

The subject of absorption was further studied in warm-blooded animals, to ascertain whether the state of the stomach and system would affect the activity of the poison. It has already been mentioned, in the early part of this essay, that Fontana and Bernard had noticed that during digestion woorara could be ingested with an impunity which did not exist in the fasting animal. This statement we have found to hold good as regards rabbits to whom vao had been given during a fast or during digestion. Those who were not digesting always died. This is the more curious because the stomach of the rabbit is never empty, and the mere fact of the mixture of the poison with the food cannot therefore be supposed to be the protective influence. M. Bernard finds an explanation of these curious facts in the circumstance that woorara, placed in contact with the outer wall of the mucous coat of a fresh stomach, will not pass through it to a solution of sugar on the other side of the membrane. The water in which the woorara is dissolved alone endosmoses to the syrup, and the poison is left behind. It is to be presumed that the mucous coat of the fasting stomach would permit of the passage of the poison; but as M. Bernard does not tell us in what functional condition were the stomachs when removed for his experiments, we are still somewhat in the dark.

It may be well to remark, in confirmation of M. Bernard, that the rule of protection is not absolute and without exception in animals who are

digesting, since, when large doses—as one-fourth to one-half a grain—of vao are used, a death sometimes occurs even where a full meal has been previously taken.

Two very interesting experiments were made to ascertain whether the condition of the system of the rabbit, as regards water, would be found to modify the facts just stated.

Expt. At different periods two large rabbits were kept on hay and corn, and without water, for nine days. At the close of that time they were deprived of food during twenty-four hours. A feed of hay was then allowed them, of which they ate greedily. An hour and a half later in one case, and two hours later in the other, they were obliged to swallow respectively one-fourth and one-half a grain of vao broken into coarse powder. They were then allowed to drink freely. Neither animal suffered. One of them was killed three days afterwards, by introducing a minute morsel of vao under his skin. The other (seven days later) is still alive. We regret that our engagements oblige us to defer the fuller consideration of this interesting subject to another occasion, when we hope to be able to offer to the Department a more satisfactory explanation of the facts above stated than has been hitherto given.

Circulation and Respiration.—The following statements of experiments upon the effects of vao on the cardiac and respiratory movements are selected as illustrations from upwards of twenty separate records of distinct experiments upon frogs and warm-blooded animals:—

Expt. A frog of middle size was selected, and the heart exposed by cutting out a triangular piece of the front of the thorax. His heart was beating forty-eight per minute, and with great regularity. After a short lapse of time, to permit any excitement consequent upon the operation to subside, the pulse was again noted at forty-eight, and a morsel of vao was placed in a small cut in the liver. In fifteen minutes the heart pulse fell to thirty-two. Three minutes later it was twenty-seven. Again, in three minutes longer the ventricle, after some irregular movements, ceased to act. Five minutes later the auricles were beating three times a minute, and the respiratory motions of the under jaw continued. Forty-seven minutes from the time at which the vao was inserted the auricular motions also ceased. The respiratory efforts were still visible, although very feeble. The heart still responded to the galvanic stimulus for upwards of twenty-five minutes. After the heart had ceased to act the frog leaped about actively, and seemed in no respect the worse for the operation until a longer period had passed by.

Expt. A large frog received a morsel of vao under the skin of his back. At the close of forty minutes we exposed the heart. It was beating twenty per minute. Ten minutes later the auricles alone acted, and shortly afterwards all motion ceased, although the frog was still active. The auricles continued to respond to galvanism, by single beats, during another half hour. At this time the nerves and muscles were still irritable to mechanical stimulus and to that of galvanism.

Expt. A small frog received in his back a morsel of vao. At the close of an hour his heart was exposed; the ventricle beat feebly ten per minute. Ten minutes later the auricles alone moved. Again, in five minutes these also were at rest, although the whole heart responded well to galvanization during forty minutes longer. The nerves continued irritable some time after the heart ceased beating, and the muscular irritability elsewhere survived that of the heart.

Expt. A large frog was poisoned by injecting a solution of vao into the subcuticular sac of the belly. At the close of one hour, and while he was still active under stimulus and restive when held, the heart was exposed. It beat twenty-nine per minute. Twenty minutes later the auricles alone acted, though the ventricle responded to galvanism by single pulsations. The auricles were at rest after eight minutes more had passed, and when the extremities were becoming

affected by the vao. The auricles continued to act feebly when galvanized at intervals during the two succeeding hours, and while the nerves had entirely lost their irritability under stimulus of any kind.

The general muscular irritability long survived that of the heart. This organ was somewhat distended, the left auricle being loaded with blood, and the ventricle being also full and dark from the blood within it.

In six frogs, similarly treated, the auricles remained irritable under galvanic stimulus during periods which varied in the different cases from thirty minutes to five hours; while in other instances, and especially when the quantity inoculated was large, the heart refused to respond to galvanism so soon as its rhythmical action was at an end.

It will be seen from the cases here recorded that the heart usually ceased to pulsate before either nervous or muscular irritability was lost, and while the animal remained capable of all the usual voluntary motions. This is so remarkable in some instances that the frog was seen to seek a place of refuge, insinuating himself under the ledge of a test-tube rack, or hiding in the folds of a cloth left on the table.

The remaining observations upon the heart's action were made incidentally while studying the absorption of vao with reference to the various surfaces. Upon comparing these with the results last obtained, a very remarkable fact was observed with reference to the departure of irritability in the nerves and muscles, and the continuance of a pulse in the heart.

Since these experiments are stated more or less fully in the portion of this paper which treats of the absorption of vao, it is unnecessary to detail more than the facts which relate to the points in question.

In the cases alluded to, vao was administered to frogs by the skin, the stomach, the rectum, etc., as has already been described. Under these circumstances the phenomena moved more slowly, and death was postponed as late as twenty-four hours or more after the use of the poison. It was then observed that in some instances the heart still acted, though with great feebleness, after all movement had departed from the voluntary muscles. When it did stop, the irritability was very rapidly lost.

In warm-blooded animals the heart usually continued to beat for a short time after respiration had ceased. As usual, the ventricle stopped first, and the auricles next. In a cat the heart beat for fourteen minutes after respiration had been checked, and was irritable under galvanism for a few minutes longer; though in warm-blooded animals generally, who die of vao, this is not the case. In all of this class of hearts the organ presented the appearances commonly seen after death by asphyxia. It was also observed that the intestines were usually the seat of active peristaltic movements.

We could scarcely anticipate that the difference in the mode of introducing this poison into the system could so affect the after phenomena. It has indeed been noticed by others that convulsive motions are more common in animals poisoned by woorara when the poison is ingested than when it is inoculated, and this fact we have also verified; but that the action of the heart should be so differently affected by the two modes of administering the agent we have employed, was an unlooked-for result. It certainly ap-

pears from the experiments detailed, as well as from others which are not stated, that when vao is inoculated it checks the heart's action, and even in some cases annihilates its sensibility to direct stimulation, before the nerves and voluntary muscles have ceased to obey volition. On the other hand, when vao is absorbed from a cutaneous or a mucous surface, the phenomena march more slowly, and the frog is left a lifeless mass, to all appearance, his nerves deprived of responsive irritability, and his voluntary muscles only alive to the direct action of galvanic currents, while the heart is still beating, or is at least awake to the galvanic stimulus.

The mode in which the heart is arrested is worthy of note. In cold-blooded animals there is no primary stimulation of the heart. It beats progressively more slowly, until the ventricle acts only in parts of its bulk, and finally ceases to move. Next the auricles stop, the right pausing first. The manner in which the tissue of the heart behaves under the influence of corroval has been already described very fully. In fact, nothing can be more curious than the bulging out of the fibres of the ventricle in places. The same phenomenon occurs in poisoning by vao, though far less marked.

It now becomes important to ascertain the cause of this enfeeblement and arrest of the heart's action. After some thought, we have concluded that in this poison, as in the corroval, this arrest of movement is due to paralysis of the muscular fibres of the organ. This paralysis appears to be localized at first in spots here and there in the ventricle, and afterwards to become general. To it are due, we conceive, the curious projection of small portions of the ventricle when the poison is fully affecting the heart. That this is the cause of the phenomenon in question may be made clear by tying the aorta of a frog, when the same phenomena present themselves as the organ becomes paralyzed from the distension to which it is exposed. A very interesting demonstration of the cause of the local prominences which we have described as marking the action of these poisons on the central organ of circulation, may be obtained by galvanizing portions of the ventricle in a frog which has taken no vao. Wherever the current passes, there is seen at the next contraction of the ventricle a prominent red elevation. The galvanism seems to over-stimulate, and thus paralyze a portion of the tissue. The rest of the heart contracts as usual, and the weakened galvanized portions is filled full of blood, and puffed out above the level of the active surrounding tissues.[1]

[1] The phenomena here described are among the most curious and striking physiological facts which have come under our consideration. The appearance presented by the heart, either where vao or corroval has been used, or when alternating galvanic currents have affected its tissue, is not easily described, so as to give any clear idea of the extraordinary behaviour of the heart under these circumstances. When the current affects the whole ventricle, it becomes large, and ceases to beat. When a small portion of the ventricle is included in the circuit, this alone pauses, and at the next beat of the ventricle makes a hernia-like projection from the neighbouring tissues. The prominences so formed are of a deep red tint. At the next action of the heart they are less marked, and in each succeeding ventricular con-

Now, whether the paralysis of the heart is due to a direct effect upon its muscular tissues, or to a paralysis of the ganglia of the heart, is a question which can scarcely be solved without a previous determination of the exact cause of the heart's rhythmical action. Since, however, the muscles of the heart so soon cease to be galvanically irritable after they have ceased to move automatically, and since it can be shown that the muscles elsewhere lose irritability earlier than usual, it is probably a direct effect on the muscular fibre of the heart which causes its arrest. If, in fact, the loss of motion were due to a nerve paralysis, the muscular tissue ought to be long afterwards responsive to stimulus. Whereas this is not the case in corroval poisoning, and only so in vao poisoning to a less extent than is usual in cold-blooded animals. Judging from warm-blooded animals only, we should conclude that vao killed by asphyxiating the animal, and thus arresting the heart. Whereas it is most probable that it is the early enfeeblement of the circulation which gives rise to a co-ordinate arrest of those muscular and nervous functions which are essential to produce and sustain respiration.

We have, however, a better proof at hand to aid us in showing that the checked respiration is only a last link in the chain of causes which produce death. The frog will live for many hours without breathing otherwise than by the skin ; yet if a frog be poisoned with vao, he dies, the heart is arrested, and certainly without asphyxia having taken place. Again, in the alligator, respiration by the lungs goes on quite actively some time after the heart has ceased to move, as we have already seen to be also the case with corroval.

Respiration.—In cold-blooded animals, as the frog, and where the poison acts rapidly, the respiratory motions of the jaw, and sometimes of the flank, not unfrequently continue after the heart's movements are at an end, but the efforts thus made do not fill the lung. When the frog is poisoned through the skin or mucous surfaces, the action of the heart long survives the respiratory motions.

The fact of the continuance of efforts to breathe after the heart has entirely stopped, has been already alluded to. In the various experiments upon the effect of vao on the other functions, will be found such record of the fact as renders it unnecessary to repeat here the statements of experiments already quoted.

Calorification.—We have not thought it requisite to examine the effect of corroval upon the temperature of animals poisoned by it, because it acts with so much rapidity that it is scarcely possible the animal could lose

traction they are less and less distinct, until only a slight flush marks the spot, and this also finally disappears. To prove conclusively that these effects are due to an over-stimulation, and a consequent temporary paralysis of the affected part, it is only requisite to over-stimulate, by mechanical means, a portion of the muscular fibres of the ventricle, when the same results occur to a more or less marked extent.

enough of heat to be appreciable, before the heart stopped. For similar reasons M. Bernard did not find any change of temperature in the animals poisoned with ordinary woorara.

In the volume so often quoted, he records a single experiment upon the temperature of animals killed by woorara, and seems to entertain no doubt as to the generality of the conclusion stated in that connection. He found that in warm-blooded animals the temperature did not fall before death. Not having a specimen of the woorara used in Europe, we are unable to verify this observation, which is doubtless correct as regards that variety of poison. In fact, it slays with such rapidity, and with so little primary effect upon the circulation, that a fall of temperature is scarcely to be anticipated where the dose is large and the death sudden. Whether any other result would occur if the amount given were so small as to insure a more lingering death, we are unable to say.

In animals poisoned by vao, the period of time which elapses between the administration of the poison and the entire cessation of movement in all the muscles except that of the heart is so considerable, that the failure of the respiratory acts is gradual. In such cases, therefore, the death is at least, in part, if not wholly, a death by asphyxia, as we have already shown ; and hence a fall in temperature is naturally to be expected. The following experiments are sufficiently definite as to this point.

Expt. A gray rabbit received in the thigh a morsel of vao, at thirteen minutes after five.

Normal temperature of the rectum 101½° F. At the close of twenty-three minutes he began to chew, as though eating, gritting his teeth at intervals. His head fell forward now and then, as though he were drowsy, and was jerked up again with a quick movement, only to sink lower a moment afterwards. In twenty-eight minutes he fell on his right side, the heart beating more slowly. The eyelids next grew insensible to a touch, the pupils largely dilated, and slight convulsive motions of the ears and hind legs took place. Temperature of rectum, 97½° F. It continued to fall up to 6 P. M., when it was no longer observed. The heart was still acting at this time, beating about once in the minute.

Expt. A large and very vigorous rabbit was selected, and a thermometer oiled and introduced into the rectum, where the temperature stood at 104° F. Fifteen drops of a solution of vao in water, 3 grs. to ℥j, were then injected into the areolar tissues of the thigh, when the following series of observations were made :—

Time.	Rectal temp.	No. of respirations.
7.20	104	
7.25	103¾	104.

The temperature with which the experiment began was unusually high for the rabbit, whose normal heat is from 101° to 102½°, or even 103° F. The rabbit had, however, struggled very violently, and hence, in all likelihood, the very elevated temperature first noted, and the consequent depression when he became entirely tranquil.

Time.	Rectal temp.	No. of respirations.	
7.30	103°	128	
7.40	102¾°		
7.43	102½	128.	Struggles.
7.45	102½	96.	Head drooping.
7.47	102¼		
7.50	102	100	

Time.	Rectal temp.	No. of respirations.
7.52	102	96
7.53	101¾	80
7.55	101½	72. Slight convulsion; eyelid irritable; pupil large; general movement of the skin muscles.
7.57	101¼	Irregular and rare.
7.58	101	Respiration ceased; the skin muscles were still moving quite actively; the head fell; the pupils were dilated; the eyelid no longer irritable; the heart still beat feebly; at

Time.	Temp.
8	100¾
8.4	100¼. Pupil contracting. At 8.8 he was opened, when the heart was found to be yet beating well though feebly. The heart was very irritable to mechanical stimulus. The muscles elsewhere responded to galvanism, but not at all to mechanical irritation. Up to 9 the temperature continued to fall, when the observation terminated.

Expt. A healthy pigeon, scantily fed, had at 1.56 P. M. a rectal temperature of 106° F., a morsel of vao being placed under the skin of his thigh. The following record of temperature was obtained:—

Time.	Temperature.
1.56	106°
1.58	105
2.1	104½
2.2	104¼
2.4	104
2.6	103¼
2.8	103. When her head drooped and fell; the eye closed, and respiration stopped.
2.14	102
2.17	101
2.21	100
2.25	99
2.29	98. No rise of temperature was observed up to 3 P. M., when he was no longer observed.

It follows very plainly from these, and similar results which we do not think it requisite to quote, that the temperature of warm-blooded animals falls considerably before death occurs.

The Nervous and Muscular Systems.—The effect of vao upon the irritability of the nerves and of the voluntary muscles is best considered together, since, in the experiments upon this point, the condition of the nerves and muscles was recorded at the same time.

In this connection, it became necessary to determine, 1st. Whether the nervous irritability lasted as long as that of the voluntary muscles. 2d. Whether the poison affected the motor or sensory nerves first, or whether both were equally attacked at one and the same time. 3d. Whether, as in the poisoning by ordinary woorara, the irritability of the muscles remains for a greater length of time than it does after death by decapitation or otherwise.

Expt. A large frog received under the dorsal skin a morsel of vao. In forty minutes all volitional control had departed. The left sciatic nerve was then isolated, divided, and the ends put upon a piece of glass. When the central end was galvanized, slight twitches occurred in the other leg, showing that the power to carry impressions to the centres, *i. e.*, sensibility, was not extinct. On galvanizing the distal end of the nerve, the muscles to which it is distributed

contracted freely. Twenty minutes later both extremities of the nerve refused to obey the galvanic irritation, although the muscles were still excitable by direct irritation.

Expt. Four hours after a morsel of vao was placed under the skin of a frog he was motionless, and no reflex motions could be obtained, except in the eyelids. At this time the left sciatic nerve was cut across. Galvanic irritation of the digital end had no effect on the muscles, which, however, continued irritable when directly galvanized during seventeen and a half hours.

Expt. A frog was poisoned like the one last described. His heart ceased beating in thirty minutes, when the nerves were still irritable. Their vitality, however, rapidly diminished and was gone in two hours, the muscles remaining alive to galvanic irritants during fourteen hours only.

Expt. A frog received in his back a small piece of vao. In forty minutes the voluntary motions were lost, and feeble reflex actions could still be provoked by pinching the legs. The eye was still irritable. At this moment the right sciatic nerve was isolated and divided without causing muscular motions in the leg. On galvanizing the centrally connected end of the nerve, one slight movement took place in the other leg. Irritation of the digital end of the nerve produced slight twitches in the peroneal muscles. Thirty minutes later both ends of the nerve were no longer irritable. The heart and muscles were still contractile when galvanized, but not when mechanically stimulated. The left leg and the rest of the body of the frog were then carefully protected by damp cloths; a dead frog being laid upon the leg on which we had operated in order to guard it from the direct effects of the moisture. In despite of these precautions, the nervous and muscular irritability was totally extinct at the close of forty-eight hours.

Expt. A large frog received in the peritoneal cavity one drachm of the weak solution of vao, one grain to one ounce, his right femoral artery having been previously tied so as to prevent the poison from having access to the tissues of this limb. The right leg now moved with more difficulty than the left. One hour and twenty minutes after the poisoning both sciatic nerves were divided. On galvanizing them both, the muscles of the leg whose artery was tied moved freely—the nerve of the uninjured leg being galvanized, feeble motions occurred in the muscles. Half an hour later the nerve of the uninjured side lost the power to evolve movement in the muscles, while galvanic irritation of the leg whose artery was tied gave rise to free motion in its muscles. The part which was protected from the poison by having its artery tied, therefore retained the irritability of its motor nerves longer than the part which was exposed to the poison. On dividing the spinal column, half an hour later, in this frog, and thrusting a probe upwards, the eyes alone moved; when the probe was thrust downwards no motion resulted.

Expt. A large frog received in his back, under the skin, fifteen drops of a solution of vao, of the strength of five grains to one ounce of distilled water. At the close of three hours, the nerves of the leg were cut across and galvanized at the digital end, causing some movement in the muscles of the calf and foot. The muscular irritability was already enfeebled. An hour later the motor nerves had lost all irritability, while the muscles were so much enfeebled that they responded but slightly when directly galvanized. The muscles of the under jaw remained irritable longer than any others, and this is usually the case in poisoning by vao.

It becomes sufficiently clear from the foregoing experiments, that under the influence of vao, the irritability of the motor nerves in the frog is lost very early, and that the irritability of the muscles is also enfeebled and finally destroyed much sooner than is usual.

It is also clear that in frogs which are poisoned rapidly by a large dose of vao, the nerves of motion cease to functionate before the muscles are deprived of the power to respond to direct stimulus—another proof, if any

were needed, of the independence of the muscular irritability, and of its absolute want of connection with that of the nerves.

To make the matter more perfectly clear and definite, a number of comparative experiments were made.

Expt. A frog was poisoned with the vapour of ammonia. At the end of twenty-four hours none of his muscles were irritable. They were not examined earlier than this.

Expt. A frog killed with atropine retained his muscular irritability during twenty-seven hours and thirty minutes, when the observation terminated.

Expt. Of two frogs killed by decapitation, the muscles remained irritable in one during thirty-nine, and in the other during forty-eight hours.

Like results were obtained in all cases of death by decapitation. Now it is well worthy of remark that on comparing our own researches upon this special point with those of the French observers, it is seen that the normal irritability of the muscles is less persistent in our frogs than in those used by the *savans* in question. In many instances stated by Bernard and others, the muscular irritability of decapitated frogs lasted during five or six days, whereas in no case has it remained in our own frogs after fifty hours. The temperature is one of the most important factors in this very interesting problem. In warm weather the irritability departs very early, and unfortunately M. Bernard does not state the condition of the thermometer at the time he made his experiments. Our own researches were conducted in a room whose temperature ranged during the period of our examinations from 49° to 68° F.

The determination of the fact of the early loss of muscular irritability under the use of vao, separates it widely from ordinary woorara, which, according to M. Barnard, not only does not weaken the muscle, but actually prolongs very remarkably the period during which they may be made to respond to galvanic or other stimuli.

In no instance was it found that vao affected the movement of the cilia in the frog's throat.

Having thus determined that the functions of the nerves are destroyed before those of the muscles succumb, and also that the muscular irritability is weakened and finally annihilated long before the time when the same result is observed in many other modes of death, we have yet to consider the remaining questions as to the order of abolition of function in the two great classes of nerves, motor and sensor—and as to the influence of vao upon the brain and the sympathetic system.

The woorara of European observers, according to M. Bernard, acts first upon the motor or efferent nerves, and destroys all reflex acts very early, because the efferent nerve which is first paralyzed is essential to the production of these phenomena. A frog which has taken woorara is, therefore, physiologically in the same state as one which has had the motor roots of the spinal nerves cut across. To test this with vao poison—

Expt. A large frog was selected, and a ligature tied around the right femoral artery. The voluntary actions ceased very early. The legs were sensitive to

direct galvanic stimulus. Slight reflex movements occurred in the legs, and the eyelids winked when touched. When the belly or back was galvanized, the leg in which the artery was tied responded by reflex movements. The other leg did not stir. On isolating its nerve and galvanizing the distal end, its muscles moved, though feebly. The nerve of the other leg being similarly irritated, vivacious motions took place in its muscles. The poison had gone too far and acted too rapidly to make this a satisfactory experiment. It showed doubtfully that both orders of nerves were affected to some extent, and it also indicated the greater tenacity of life in the upper part of the body, where the eyelids continued irritable and where the muscles under the jaw responded when the motor manifestations were weak in all other parts of the body exposed to the action of the vao. At the close of an hour and a half the spine was destroyed, when the leg which had been operated upon moved slightly. No other motion resulted and the muscular irritability was extinct in five hours.

Expt. A large frog poisoned by vao was motionless in three hours, save that the eyelids still acted. His left femoral artery had been previously tied. The right sciatic nerve was exposed, divided, and the two ends insulated on glass. As the poison had been cut off from the left leg, it could not share in any supposed loss of motor power, should such exist. If motion was lost in the poisoned parts and sensation remained, an irritant applied to the centric end of a nerve in the poisoned part would convey the stimulant effect to the nerve centres of the spine, and the nerve of the unaffected limb ought to acknowledge the irritation by reflex acts. The irritation of the poisoned nerve would be felt by the nerve centres, but in case the motor functions of the poisoned parts were abolished, no muscular reflex act could result anywhere, save in the unpoisoned limb, whose nerve and muscles would, so to speak, translate into the language of motion the reflected impression. Such does occur with ordinary woorara. In the present instance neither the galvanization of the fore legs nor of the centric end of the right sciatic caused motion in the unpoisoned leg, which, however, moved vivaciously when directly stimulated. A probe thrust down the spine produced free motion in the leg the artery of which was tied, and some twitches in the other. The defect of reflex motion was, therefore, not due to want of life in the motor nerves or the spinal centres.

Expt. The sciatic nerve of the left leg of a frog was isolated, and a wire being passed beneath, it was carried around the rest of the limb and tightly twisted. Vao was then employed as usual. The right brachial nerve was galvanized after the reflex motions had become extinct to all appearance—slight movements took place in the leg of the same side, but no form of stimulus applied to either brachial nerve caused motion in the leg on which we had operated. The twitches above mentioned showed, however, that both motor and sensory power was feebly preserved even in the poisoned parts. A little later no such motions could be had, although the poisoned limbs still moved for a time when their nerves were directly stimulated.

Expt. A very large frog had his sacrum removed, so as to expose the lumbar nervous plexus. A ligature was cast about the rest of the body, excluding these nerve-trunks. As the ligature arrested the circulation, the bridge of nerves alone connected vitally the two segments of the frog. A solution of vao was now injected under the skin of the trunk, above the ligature. Two hours later, the reflex acts being at an end in the upper parts of the frog, the brachial nerves were irritated, but without evolving the slightest motion in the unpoisoned limbs. Direct stimulus applied to the lumbar plexus caused free movement in the legs.

In the next experiment the brain was removed before the frog was poisoned. His reflex motions were well developed, but faded rapidly. The nerves of the arms were galvanized, and by degrees lost the power to provoke motion elsewhere; while, at the same time, their muscles still moved when the distal end of the nerve was galvanized.

Expt. A large frog was chosen, and the heart exposed. A large amount—twenty drops—of a solution of vao, five grains to the ounce, was put under the skin of the back. In fifteen minutes the ventricle stopped, and the auricles also ceased beating in twenty-five minutes. Three hours after the poisoning one sciatic nerve was uncovered and galvanized by a powerful alternating current; the

muscles of the same leg responded freely. The nerve was then cut, and the centric end galvanized, without any reflex acts occurring. The lumbar nerves were next tested, but still with no result as to reflex motion elsewhere. Finally an examination of the nerves of the other limbs showed that their nerves still retained motor power, and that their muscles were sufficiently irritable.

It becomes very clear from these experiments, and others which we cannot afford space to quote, that vao acts first upon the sensitive nerves, and not, like other woorara, upon the motor filaments. Its next action is upon the motor function of the nerve-trunks, and lastly upon the independent irritability of the muscles.

In almost all of the experiments, although the fore legs were first affected in the paralysis which finally involved all parts, the respiratory muscles under the jaw and the muscles of the eyelids remained active long after all the rest, although so feeble that their efforts did not suffice to fill the lungs.

It has been shown conclusively, in the early portions of this paper, that the mere stoppage of the circulation by ligation of the vessels at the base of the heart produced a rapid and complete loss of nervous but not of muscular irritability. The paralysis of the nervous system, under the use of vao, is therefore due, in all probability, to the enfeeblement and final loss of cardiac power. The defect of muscular irritability must be a result of the poison acting on the tissue of the muscles themselves.

Effect of Vao on the Blood.—After repeated examinations of the blood of animals killed by this poison, we have been unable to trace the slightest alteration in the form of the blood-globule when the perfectly fresh blood was inspected. If it be allowed to stand some time, either within the animal or after removal from his vessels, the usual alterations in the form of the disks may be seen. One observer, at least, has conceived that ordinary woorara affected the forms of the blood-disks; but all subsequent investigations have been opposed to this view, and it is probable that his examination of the vital fluid was delayed so long as to permit of those osmatic changes in form to which the delicate red corpuscles are so familiarly liable.

We have also studied the blood with reference to the influence of vao on its coagulation, and on its power to absorb oxygen. Neither in frogs, in rabbits, nor in birds, has vao appeared to retard the coagulation of the blood. In one single case, that of a cat, was this act unusually delayed.

In the frog and the alligator the lung appears to supply sufficient red blood up to the last moment to redden the heart in one-half of its area until the ventricle ceases to move. Where, therefore, asphyxia is not an essential result, as in these cold-blooded animals, the heart is checked by the vao before any marked change has taken place in the colour of the blood. In warm-blooded animals—cats, rabbits, mice, birds, etc.—the final link in the chain of causes which produces death is asphyxia from want of muscular movement. Here the blood is black, and the heart presents the appearances commonly observed in asphyxiated animals. The power of this dark blood to reabsorb oxygen was ascertained in the following man-

ner: The blood of a large rabbit, poisoned with vao, was whipped as it escaped into a vessel, to free it from fibrin. Thus prepared, it was agitated in a bottle with atmospheric air, when it was soon observed to have recovered its bright arterial hue.

Before we call attention to the subject of the differences between corroval, woorara, and vao, it has occurred to us that it would be as well to state here the physiological evidence bearing upon the question of what it is that gives the deadly potency to corroval and vao. A portion of such evidence is to be found in the chemical and microscopical characters of these poisons, and we shall in this place insist alone upon certain interesting physiological facts. The old opinion as to the activity of woorara being due to the venom of poisonous serpents is still to some extent a popular belief. To examine this matter anew, with reference to the poisons before us—

Expt. A large frog was chosen, and a small scale of dried venom from the rattlesnake was placed under the skin of his back. This poisonous material is nearly two years old, and is in the form of dry yellow scales upon the side of a bottle. It was obtained by one of the authors of this paper (Dr. Hammond), by holding a snake with his upper jaw over the edge of the bottle, so that, on irritation, he discharged his poison into its interior.

During twenty-five minutes the frog, poisoned as described, was unusually active. At the close of this period he became more quiet, and occasional twitches were observed in the hind legs, which were also extended spasmodically at intervals. Ten minutes later he lay quiet as placed, in any position, breathing at intervals. The eyelids were irritable, and reflex motions could be provoked. All voluntary power seemed to have fled. One hour and ten minutes later the reflex motions still occurred when irritants were used, and the twitching and extension of the legs continued. He was now becoming rapidly enfeebled. Two hours and fifty minutes after the administration of the poison no motions could be evolved, and he was then laid open. On applying the galvanic current to the voluntary muscles no motion occurred, and the nerves were, of course, unable to produce any muscular response when galvanized. The heart was still beating.

A second experiment, of a similar nature, was made upon a large frog, with nearly similar results, except that death did not occur until five hours after the venom was used. It was noted in this case, as a curious fact, that the eyelids were insensible before the reflex movements of the extremities were lost. After all reflex motion had departed, the heart, which was large and almost black, continued to act during more than two hours in all of its cavities. During this time the nerves and muscles were more or less irritable when galvanized. The vitality of both nerves and muscles was lost within five hours after the heart had ceased to act.

These two cases differ from one another in certain particulars which demand the future criticism of experiment; but at present it is enough to point out the dark and swollen state of the heart, its long-continued and perfect action in all its parts, and the occurrence in both frogs of local spasms of the muscles, as well as occasional convulsive extensions of the hind legs, as marking a difference between the venom and both corroval and vao, which we hope to examine more fully at another time.

It might naturally be supposed that the local character of the wounds would also constitute a further ground of distinction. We were not astonished, however, to observe that the rattlesnake poison produced no local effect in the frog. The wound in which was placed vao, corroval, or the dried

venom of the *Crotalus confluentus* was not in any way to be distinguished by the eye. Meanwhile, it is to be observed that the animals used were cold-blooded reptiles, which are not capable of developing inflammatory action, such as is observed in the tissues of mammals similarly treated.

Again, it is worthy of note that the venom employed was two years old, and perfectly dry. How far this may have modified the result we are as yet unable to say. A pigeon, poisoned with the dried venom of the crotalus, died in two hours and fifty-two minutes. Two minutes after the wound was made in his thigh it had become black. Around this a ring of a deep amber colour was seen, and before death a dark serous fluid exuded from the wound. A simple wound made at the same time exhibited no such phenomena. Very little swelling occurred about the poisoned wound, and no general swelling of the body was observed. Soon after the inoculation was effected the pigeon rocked on his feet, staggered, fell, and rose again, flapping his wings and vomiting corn from the crop. A half hour later he gradually sank down, the breathing grew laboured and uneasy, and the heart beat rapidly. The temperature fell to 94° F. one hour and thirty-two minutes after the poisoning, and continued to fall, until, when it reached 88° F., death occurred, during general but not very violent convulsions. Rigor mortis came on within forty-two hours. On examination of the blood-globules, they presented no unusual or abnormal peculiarities. The local affection is in this warm-blooded bird the distinctive difference between the action of vao or corroval and that of the serpent poison. In both cases asphyxia is in warm-blooded animals the last link in the chain of causes which produce death.

It is, then, highly improbable that the venom of serpents is used in the manufacture of the poisons before us. As it is stated that ordinary woorara is formed from the juice of the *Strychnos toxifera*, and as the alliances of this plant would seem to make it probable that it contained strychnia, it became interesting to know whether that substance might not have been so altered by the long boiling required to prepare the woorara as to change its character and affect its toxicological peculiarities. Accordingly a grain of strychnia was boiled with gum starch and water for nine hours, without in the least impairing its peculiar qualities. A frog poisoned with the mixture died, tetanized as usual. We desired to ascertain, in the next place, whether, if our own vao poison contained strychnia, it would be so modified by the other constituents of the poison as to lose its peculiar powers. A minute portion of strychnia was therefore added to a little vao, and the two poisons inserted under the skin of a frog. He perished in tetanic spasms, and the heart stopped soon after death. The same effects were observed when corroval and strychnia were separately introduced under the skin in two distinct localities. Now, as the heart of the strychnized frog will beat for some hours after all externally visible motion has ceased, it is plain that in the double poisoning both agents produced their own distinct and pecu-

liar effects. The one caused tetanic spasms, the other paralyzed the heart. It is, therefore, sufficiently clear that no form or modification of strychnia is present in the vao or corroval.

In addition to the negative evidence here adduced, we have the more positive results which have been stated in connection with the physical and chemical examination of the two poisons. From the whole evidence, we feel authorized in considering both poisons as of vegetable origin.

The history of the antidotes to this poison may be very shortly summed up.

Sir Walter Raleigh, in his very curious account of the arrow-poison, tells us that the Spaniards were cured of ordinary poisoned wounds by the use of the juice of the garlike (garlic), in which, however, he reposes but little faith. His own remedy, a knowledge of which he professed to have obtained from the Indians, he thus describes: "But this is a general rule for all men that shall hereafter travell the Indies, where poisoned arrows are vsed, that they must abstaine from drinke, for if they take any licor into their body, as they shall be marvellously provoked thereunto by drought. I say if they drink before the wound be dressed, or soone vpon it, there is no way with them but present death."[1] The next allusion to antidotes is equally vague, and it is even doubtful whether the poison alluded to has any analogy to the woorara at present known, since it is said by the authority referred to, that it kills only after seven days. De la Vega further informs us that to arrive at a knowledge of the antidote, the Spaniards wounded an Indian with a poisoned arrow, and then setting him free, observed that he chose certain herbs, which he ate, and applied locally, with entire success.[2]

De la Condamine[3] is the first writer who speaks of sugar and salt as antidotes. After returning to Cayenne, he made a few experiments with woorara, thirteen months old. Of two chickens which were poisoned by woorara, and treated with sugar internally, one died. Afterwards, at Leyden, and before Mussenbreck, Van Swieten, and Albinus, the sugar antidote totally failed. Some of De la Condamine's woorara passed into the hands of M. Hérissant,[4] who used sugar and wine as antidotes in the case of a lad who had been left to watch some of the poison which was boiling in a small and close room. The boy became weak, and was supposed to have been a sufferer from the poisonous fumes. It is needless to add that in his case the sugar acted perfectly. Not so fortunate were ten birds which were poisoned by M. Herissant, with a mixture of Lamas and Ticunas, and instantly fed upon sugar. Nine of them perished. Salt

[1] Sir W. Raleigh. Disc. of Guiana, p. 71.
[2] The Royal Commentaries of Peru. By the Inca Garcilasso de la Vega. London, 1688, p. 741.
[3] Tr. de l'Acad. des Sci., 1745, vol. lxii. p. 489.
[4] Phil. Trans., vol. xlvii. p. 75. 1746.

proved equally unsuccessful, whereas instant amputation, or the actual cautery, saved the life of the animal. A single experiment was made as to the value of the ligature as a safeguard. Although applied to the limb beforehand, it failed entirely. M. Hérissant also essayed the effect of large bleedings, after the poison had been given to horses. Of six so treated, two recovered.

Schomburgk,[1] whose work is of comparatively recently date, repeats the old story of sugar and salt as antidotes, adding, that the whites alone repose confidence in their protecting power. The Indians, who are said to place but little reliance upon any of the supposed antidotes, mention, as the best, cane-juice (sugar) alone or mixed with an infusion of the root of the wallabo (eperua or dimorpha).

Bancroft[2] relates that " the white inhabitants of Guiana consider sugar, *i. e.*, cane-juice, as a remedy in poisoning by the acawau, a variety of woorara. The Indians themselves do not acknowledge this property of the cane, and," he adds, " I have never been able, either by my own experiments or inquiries, to discover a single instance of its efficacy for that purpose.

With Fontana[3] began the closer examinations of this singular poison, which have made its modern physiological history a matter of such deep interest. This observer found that when the mineral acids were mingled with the Ticunas poison, it was rendered innocuous as an injection under the skin, or as a local application upon the bare muscles. The same result ensued when the acids were evaporated with the poison, and the residue was employed. Neither vinegar nor rum were of any avail as antidotes, when mixed with the Ticunas.

Osculati[4] also alludes to the antidotes, and states that a mixture of salt and sugar acts as such when taken freely, but that it is also essential to place in the wound a weapon dipped in this mixture, and to continue taking the not very agreeable compound of dissolved salt and sugar for some time afterwards. This statement is mere hearsay, and rests upon no experiments by the author of the paper in question.

The experiments of Drs. Brainard and Green, first in Chicago, and afterwards in Paris,[5] lead these gentlemen to consider the mixture of iodide of potassium and iodine as an antidote, when mingled with the poison in solution. These experiments are quoted and commented upon by Dr. Green himself, in a paper on woorara, which he has written since the date of the communication to the Academy, of his own results, and those of Dr. Brainard.[6] The last named researches shortly afterwards elicited from M. Reynoso an admirable paper[7] upon the use of various agents as antidotes

[1] Schomburgk, 1847.
[2] Bancroft, p. 297.
[3] Fontana, vol. xi. p. 118. 1781.
[4] Osculati, p. 201. 1850.
[5] Comptes Rendus de l'Acad., vol. xxxviii. p. 411. 1854.
[6] Am. Med. Gaz., vol. vii., Nos. 5 and 7; vol. vii., No. 1; 1855–6.
[7] Reynoso. Comptes Rendus de l'Acad., vol. xxxix. p. 68. 1854.

to woorara. In reviewing the essay of Drs. Brainard and Green, he classes as a caustic the iodine solutions employed by these gentlemen. He, therefore, attempted to render the iodine harmless to the tissues, while securing its primitive action upon the woorara. Having found that iodide of potassium used alone with woorara solution, did not prevent, but merely delayed its ultimate manifestations, he made the following experiments :—

Half a gramme of iodide of potassium, and 0.4 gramme of iodine, with 0.06 gramme of curare in solution were treated with hyposulphite of soda, drop by drop, until the iodine disappeared, when the mixture was rendered alkaline by the addition of carbonate of soda. This mixture killed in twenty minutes, when injected under the skin. A mixture of alcohol, iodine and curare did not prove fatal; but when, in such a mixture, the iodine was rendered inactive, by the use of the hyposulphite of soda, poisoning followed its use, in one hour and forty minutes. M. Reynoso thence concludes that iodine alters the poison, but does not destroy it. Hypochlorite of lime also delayed the action of the woorara. Experiments were further instituted, which seem to show that chlorine in a nascent or free state, destroys the poison. Chloride of sodium mingled with it did not save the animals tested with this mixture.

In another series of experiments, the author added 10 gtt. of bromine to 0.06 gramme woorara, and 7 cubic centimetres of water. This mixture was rendered fully alkaline by carbonate of soda and some few drops of hyposulphite of soda were added. It was injected into the subcuticular tissues of an animal, who died in 24 hours, in collapse, poisoned by the bromide of sodium, which, used alone, was found to be fatal in a like dose. When a mixture of woorara and bromine was heated until the bromine escaped, the residue was harmless when injected into animal tissues.

Sulphuric and nitric acids, caustic potash, lime-water, and ammonia-water, all retarded the action of woorara when mixed with it. Certain salts which are not caustic, such as the iodide and bromide of sodium, and iodide of potassium, also exercise a retarding influence; but this effect M. Reynoso looks upon as undoubtedly local, since iodide of potassium, given internally, does not prevent the poison from proving active when afterwards used subcutaneously. Both Messrs. Brainard and Green, and M. Reynoso are of opinion that the application of the cupping-glass, so long as it is kept applied, prevents the poison from being absorbed.

Notwithstanding the ingenuity of M. Reynoso's experiments, they do not entirely settle the question of antidotes to woorara, and while the action of certain salts in delaying the absorption, or the after-action of the poison, is distinctly made out, we are still left in the dark as to the cause of this effect from the use of an agent so harmless as iodide of potassium. Even upon M. Reynoso's showing, the solution of iodized iodide of potassium used by the American experimenters would have the double advantage of a cauterizing and a delaying agency when used with the poison, or put instantly upon the wound.

With woorara, as in many other kinds of poisoning, artificial respiration maintained for a length of time, saved the animal, when the dose of the poison was not overwhelming. Waterton's experiments on this subject are very striking, and are the last to which we shall refer, since the very recent writers, as Kölliker and Bernard, have merely quoted their facts from M. Reynoso's paper, which we have already analyzed. It is unnecessary to quote here the simple experiments which satisfied us that neither

sugar nor salt has any claims to be regarded as antidotes. Since, however, Brodie, Waterton and others had previously found, that by sustaining artificial respiration, time was allowed for the elimination of the woorara, and the animal escaped death, we resorted to the same expedient in rabbits and cats poisoned by corroval and vao. In no instance was the death even so much as retarded, and the heart ceased to beat as soon as usual. This result could have been anticipated, from the fact that in the alligator thus poisoned, respiration continued perfect long after all cardiac movement had departed. In one sense, therefore, corroval and vao are more deadly agents of destruction than common woorara, since, for them, no physiological antidote of any kind exists, while in poisoning by woorara, at least one resource is available.

Conclusions.—1. Vao, either in a solid, or more quickly in a liquid form, can be absorbed from the areolar tissues of cold-blooded animals as the frog.

2. It is also absorbed by the stomach, œsophageal mucous membrane, rectum, and skin, with a degree of rapidity which varies, and is rapid or slow as the animal is ill or well supplied with water.

3. Warm-blooded animals absorb vao from the stomach and intestine when they are fasting, but suffer no ill effects when the vao is given during digestion. That this protection is not due to a mere mixture of the vao with the food of the full stomach, is shown by the fact that rabbits, whose stomachs are always more or less distended with food, are protected only when owing to the entry of fresh food, digestion becomes active.

4. The demands of the system for water do not affect to any perceptible extent the absorption of vao from the stomach of the rabbit.

5. The circulation of the frog is arrested within from ten minutes to one hour by the introduction of vao under the skin. The same result obtains within from twenty-four to forty-eight hours, when the poison is swallowed in small doses.

6. The first effect of vao is to increase the force of the heart without increasing the number of its pulsations.

The next effect is a paralysis of the muscular tissues of the heart, so that the ventricle stops first and the right and left auricles next, in the order in which they are named. In a majority of the frogs poisoned by vao, the heart remained galvanically irritable for a certain time after the organ had ceased to pulsate.

The heart stops before the voluntary motions are at an end, in all cases of rapid poisoning. When poisoning occurs by absorption from a mucous surface, the phenomena march more slowly, and voluntary control and reflex power are sometimes lost before the heart has entirely ceased to beat.

7. Vao stops the respiration in warm-blooded animals by arresting the circulation, and so paralyzing the nervous system, without which respira-

tion is impossible, so that the checked respiration is a consequence and not a cause of the injury to the cardiac functions.

In the batrachia also, the respiratory movements cease before the heart has entirely lost the power to pulsate.

In the alligator poisoned by vao the respiration is perfect some time after the heart is at rest.

8. The facts last quoted and the inability of artificial respiration to restore or sustain the cardiac movements in warm-blooded animals poisoned by vao, proves sufficiently that the first effect of the poison is upon the heart, and that the appearances of asphyxia observed post-mortem in rabbits, cats, etc., are of secondary importance so far as concerns the cause of death.

9. The temperature of warm-blooded animals poisoned by vao falls with considerable rapidity, and does not undergo any elevation after death.

10. The nerves of sensation first lose their power to convey impressions—the motor nerves are next affected. The paralysis of the nerves extends from the periphery to the centre. The affection of the nervous system may be due to the sudden arrest of the circulation, and not of necessity to the direct influence of the vao. The irritability of the voluntary muscles in the frog is lost much earlier than is the case when the animal dies by decapitation.

11. The sympathetic nerve is paralyzed, at least in the upper portion of its distribution, before the nerves elsewhere have lost their functional power.

12. The ciliary motion is unaffected by the use of vao.

13. The blood of animals thus poisoned coagulated as usual, and had not lost the power of changing colour when exposed to oxygen or carbonic acid.

14. So far as we are aware, no true physiological antidote exists for vao poison, since even artificial respiration fails to sustain life in animals affected by it.

15. The vao poison closely resembles corroval in its physical, chemical, and physiological reactions. The alkaloids extracted from the two poisons produce in animals of equal size effects which cannot be distinguished.

We, therefore, are inclined to consider vao as merely a weaker variety of corroval, and to conclude that the apparent difference in the effects produced by the original extracts is due to a difference in their strength.

We have thus brought to a close an investigation which has involved considerable labour, and we now submit our results for the consideration of the Department. No statement has been made in this essay, and no conclusion deduced, of the accuracy or truth of which we at least are not fully satisfied. How far this may be the case with others we cannot say; and, at all events, whatever be the fate of these researches, we shall at least have had the pleasure of the pursuit, and the satisfaction of stimulating

inquiry upon questions of interest and importance. With the words of the venerable Abbé Fontana, whose labours in the field of biological investigation have been too much neglected, we would say, in conclusion, "Those only who observe and experiment make mistakes, those only who do neither, never err."

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